```
                        GenCore version 5.1.6
              Copyright (c) 1993 - 2004  Compugen Ltd.



OM protein - protein search, using sw model

Run on:          January 21, 2004, 09:14:54 ; Search time 2.63862 Seconds
                                             (without alignments)
                                             601.551 Million cell updates/sec


Title:           US-09-869-414A-64
Perfect score:   49
Sequence:        1 SEVKMDAEFR 10


Scoring table:   BLOSUM62
                 Gapop 10.0 , Gapext 0.5


Searched:        1107863 seqs, 158726573 residues


Total number of hits satisfying chosen parameters:       1107863


Minimum DB seq length: 0
Maximum DB seq length: 2000000000


Post-processing: Minimum Match 0%
                 Maximum Match 100%
                 Listing first 45 summaries


Database :       A_Geneseq_19Jun03:*
                 1:   /SIDS1/gcgdata/geneseq/geneseqp-embl/AA1980.DAT:*
                 2:   /SIDS1/gcgdata/geneseq/geneseqp-embl/AA1981.DAT:*
                 3:   /SIDS1/gcgdata/geneseq/geneseqp-embl/AA1982.DAT:*
                 4:   /SIDS1/gcgdata/geneseq/geneseqp-embl/AA1983.DAT:*
                 5:   /SIDS1/gcgdata/geneseq/geneseqp-embl/AA1984.DAT:*
                 6:   /SIDS1/gcgdata/geneseq/geneseqp-embl/AA1985.DAT:*
                 7:   /SIDS1/gcgdata/geneseq/geneseqp-embl/AA1986.DAT:*
                 8:   /SIDS1/gcgdata/geneseq/geneseqp-embl/AA1987.DAT:*
                 9:   /SIDS1/gcgdata/geneseq/geneseqp-embl/AA1988.DAT:*
                 10:  /SIDS1/gcgdata/geneseq/geneseqp-embl/AA1989.DAT:*
                 11:  /SIDS1/gcgdata/geneseq/geneseqp-embl/AA1990.DAT:*
                 12:  /SIDS1/gcgdata/geneseq/geneseqp-embl/AA1991.DAT:*
                 13:  /SIDS1/gcgdata/geneseq/geneseqp-embl/AA1992.DAT:*
                 14:  /SIDS1/gcgdata/geneseq/geneseqp-embl/AA1993.DAT:*
                 15:  /SIDS1/gcgdata/geneseq/geneseqp-embl/AA1994.DAT:*
                 16:  /SIDS1/gcgdata/geneseq/geneseqp-embl/AA1995.DAT:*
                 17:  /SIDS1/gcgdata/geneseq/geneseqp-embl/AA1996.DAT:*
                 18:  /SIDS1/gcgdata/geneseq/geneseqp-embl/AA1997.DAT:*
                 19:  /SIDS1/gcgdata/geneseq/geneseqp-embl/AA1998.DAT:*
                 20:  /SIDS1/gcgdata/geneseq/geneseqp-embl/AA1999.DAT:*
                 21:  /SIDS1/gcgdata/geneseq/geneseqp-embl/AA2000.DAT:*
                 22:  /SIDS1/gcgdata/geneseq/geneseqp-embl/AA2001.DAT:*
                 23:  /SIDS1/gcgdata/geneseq/geneseqp-embl/AA2002.DAT:*
                 24:  /SIDS1/gcgdata/geneseq/geneseqp-embl/AA2003.DAT:*


       Pred. No. is the number of results predicted by chance to have a
       score greater than or equal to the score of the result being printed,
```

and is derived by analysis of the total score distribution.

SUMMARIES

Result No.	Score	% Query Match	Length	DB	ID	Description
1	49	100.0	10	13	AAR24261	Human amyloidin pr
2	49	100.0	10	21	AAY69703	Beta-APP alpha-sec
3	49	100.0	10	22	AAE10654	Human wild-type AP
4	49	100.0	10	22	AAE06899	Human amyloid prec
5	49	100.0	10	22	AAU06628	Asp2 recognition s
6	49	100.0	10	22	AAU07227	Human beta-amyloid
7	49	100.0	10	22	AAE02606	Human wild-type AP
8	49	100.0	10	22	AAB66574	Synthetic peptide
9	49	100.0	10	22	AAB46208	Human APP derived
10	49	100.0	10	22	AAB61336	Sythetic peptide f
11	49	100.0	10	23	ABG78375	Human beta amyloid
12	49	100.0	10	23	ABG30940	Nogo/BACE method c
13	49	100.0	10	23	AAU99490	Peptide #1 used as
14	49	100.0	10	23	ABB78615	Beta-secretase spe
15	49	100.0	10	23	ABB06426	Human APP beta-sec
16	49	100.0	10	24	ABG76103	Amyloid precursor
17	49	100.0	11	22	AAB75143	APP beta-secretase
18	49	100.0	11	22	AAB75144	Asp 1 substrate se
19	49	100.0	11	22	AAB97468	Asp2 substrate wil
20	49	100.0	12	23	ABB08997	Amyloid precursor
21	49	100.0	12	23	ABB07592	Biotinylated synth
22	49	100.0	12	23	AAE16657	APP substrate pept
23	49	100.0	12	23	AAU74831	Synthetic amyloid
24	49	100.0	12	24	AAO26795	Beta-secretase sub
25	49	100.0	13	19	AAW70869	Beta-amyloid pepti
26	49	100.0	13	23	AAM50891	Fluorescent substr
27	49	100.0	13	24	ABP71624	Beta-secretase act
28	49	100.0	13	24	ABG75934	Synthetic Amyloid
29	49	100.0	13	24	ABP71462	Beta-secretase act
30	49	100.0	13	24	ABP71263	Synthetic APP subs
31	49	100.0	13	24	AAO16443	Beta-secretase syn
32	49	100.0	13	24	ABP57078	Synthetic amyloid
33	49	100.0	13	24	ABP58369	Synthetic amyloid
34	49	100.0	16	21	AAB06315	Human beta-amyloid
35	49	100.0	16	21	AAB06317	Human beta-amyloid
36	49	100.0	18	22	AAE00608	Beta-amyloid precu
37	49	100.0	20	21	AAY69713	Beta-APP alpha-sec
38	49	100.0	23	22	AAB75147	Asp 1 substrate se
39	49	100.0	23	22	AAB97473	Asp2 substrate wil
40	49	100.0	33	20	AAW98002	Amyloid precursor
41	49	100.0	39	21	AAY69717	Beta-APP alpha-sec
42	49	100.0	45	18	AAW26512	Amyloid precursor
43	49	100.0	45	18	AAW26392	Amyloid precursor
44	49	100.0	45	19	AAW44748	APP-REP 751 [BAP d
45	49	100.0	45	19	AAW42977	Deletion beta-amyl

ALIGNMENTS

RESULT 1
AAR24261
ID   AAR24261 standard; Protein; 10 AA.
XX
AC   AAR24261;
XX
DT   25-MAR-2003 (updated)
DT   09-NOV-1992 (first entry)
XX
DE   Human amyloidin protease substrate sequence #1.
XX
KW   Alzheimer's disease; beta amyloid precursor protein; APP; zinc;
KW   metalloprotease; hAP; protease inhibitor; APP592-601
XX
OS   Synthetic.
XX
FH   Key   Location/Qualifiers
FT   Modified-site   1
FT   /note= "Acetylated-Ser"
XX
PN   WO9207068-A1.
XX
PD   30-APR-1992.
XX
PF   04-OCT-1991;   91WO-US07290.
XX
PR   05-OCT-1990;   90US-0594122.
PR   30-SEP-1991;   91US-0766351.
XX
PA   (ATHE-) ATHENA NEUROSCIENCES INC.
PA   (ELIL) LILLY & CO ELI.
XX
PI   Dovey HF,   Johnstone EM,   Little SP,   McConlogue L,   Seubert PA;
PI   Sinha S;
XX
DR   WPI; 1992-167148/20.
XX
PT   Human amyloidin protease - used for cleaving Met-Asp bond in
PT   amyloid-like substrate for identifying protease inhibitors
XX
PS   Claim 1; Page 52; 62pp; English.
XX
CC   Claimed human amyloidin protease is defined by its ability to
CC   cleave the Met-Asp bond of this synthetic substrate. The substrate,
CC   which corresponds to residues 592 to 601 of the 695 amino acid APP,
CC   can be used in an assay for identifying inhibitors of proteases
CC   which cleave Met-Asp bonds, e.g. amyloidin, human skin chymase or
CC   rat mast cell protease I or II.
CC   See AAR24260-3, AAR24266-7 and AAQ24875-Q24887.
CC   (Updated on 25-MAR-2003 to correct PN field.)
XX
SQ   Sequence   10 AA;

    Query Match   100.0%; Score 49; DB 13; Length 10;
    Best Local Similarity 100.0%; Pred. No. 0.00059;
    Matches   10; Conservative   0; Mismatches   0; Indels   0; Gaps   0;

```
Qy        1 SEVKMDAEFR 10
            | | | | | | | | | |
Db        1 SEVKMDAEFR 10
```

RESULT 2
AAY69703
ID   AAY69703 standard; peptide; 10 AA.
XX
AC   AAY69703;
XX
DT   11-APR-2000   (first entry)
XX
DE   Beta-APP alpha-secretase substrate [KMD]-APP(-5,+5).
XX
KW   Nootropic; neuroprotective; beta-amyloid precursor protein; metabolism;
KW   cleavage site; beta-secretase; neurodegenerative disease;
KW   Alzheimer's disease.
XX
OS   Homo sapiens.
XX
PN   WO9964587-A1.
XX
PD   16-DEC-1999.
XX
PF   04-JUN-1999;   99WO-FR01326.
XX
PR   05-JUN-1998;   98FR-0007068.
PR   31-MAR-1999;   99US-0122599.
XX
PA   (RHON) RHONE-POULENC RORER SA.
PA   (UYPA-) UNIV CURIE PARIS VI P & M.
XX
PI   Rholam M, Munoz-Gimenez N, Moutaouakil M, Cohen P, Bertrand P;
XX
DR   WPI; 2000-097537/08.
XX
PT   Polypeptide with beta-secretase activity, specific for wild-type
PT   amyloid precursor protein, useful in treating Alzheimer's disease -
XX
PS   Example 3; Page 24; 44pp; French.
XX
CC   Peptides AAY69702-Y69718 represent synthetic peptide substrates for a
CC   novel polypeptide with beta-secretase activity that can cleave
CC   specifically the natural beta-amyloid precursor protein (bAPP). Normal
CC   cleavage of the protein occurs between amino acids Met596-Asp597 and
CC   Val636-Ile637 (positions 4-5 and 44-45 of AAY69701). The novel
CC   polypeptide is used to identify agents that interact specifically with
CC   it. These agents regulate metabolism of APP, particularly they slow down
CC   or reduce production of beta-amyloid, so can be used to treat
CC   neurodegenerative diseases, particularly Alzheimer's disease.
XX
SQ   Sequence   10 AA;

  Query Match   100.0%; Score 49; DB 21; Length 10;
  Best Local Similarity   100.0%; Pred. No. 0.00059;
  Matches   10; Conservative   0; Mismatches   0; Indels   0; Gaps   0;

```
Qy      1 SEVKMDAEFR 10
          | | | | | | | | | |
Db      1 SEVKMDAEFR 10
```

RESULT 3
AAE10654
```
ID   AAE10654 standard; peptide; 10 AA.
XX
AC   AAE10654;
XX
DT   10-DEC-2001  (first entry)
XX
DE   Human wild-type APP beta-secretase peptide, PHA-95812E.
XX
KW   Human; aspartyl protease 1; Asp1; amyloid precursor protein;
KW   Alzheimer's disease; AD; dementia;  neurofibrillary tangle; gliosis;
KW   amyloid plaque; neuronal loss; proteolytic; nootropic; neuroprotective;
KW   APP beta-secretase peptide.
XX
OS   Homo sapiens.
XX
FH   Key              Location/Qualifiers
FT   Cleavage-site    5..6
XX
PN   GB2357767-A.
XX
PD   04-JUL-2001.
XX
PF   22-SEP-2000; 2000GB-0023315.
XX
PR   23-SEP-1999;    99US-0155493.
PR   23-SEP-1999;    99US-0404133.
PR   23-SEP-1999;    99WO-US20881.
PR   13-OCT-1999;    99US-0416901.
PR   06-DEC-1999;    99US-0169232.
XX
PA   (PHAA ) PHARMACIA & UPJOHN CO.
XX
PI   Bienkowkski MJ,  Gurney M;
XX
DR   WPI; 2001-444208/48.
XX
PT   Polypeptide comprising fragments of human aspartyl protease with
PT   amyloid precursor protein processing activity and alpha-secretase
PT   activity, for identifying modulators useful in treating Alzheimer's
PT   disease -
XX
PS   Example 12; Page 84; 187pp; English.
XX
CC   The patent discloses human aspartyl protease 1 (hu-Asp1) or modified
CC   Asp1 proteins which lack transmembrane domain or amino terminal
CC   domain or cytoplasmic domain and retains alpha-secretase activity
CC   and amyloid protein precursor (APP) processing activity. The proteins
CC   of the invention are useful for assaying hu-Asp1 alpha-secretase
CC   activity, which in turn is useful for identifying modulators of
```

CC   hu-Asp1 alpha-secretase activity, where modulators that increase
CC   hu-Asp1 alpha-secretase activity are useful for treating Alzheimer's
CC   disease (AD) which causes progressive dementia with consequent
CC   formation of amyloid plaques, neurofibrillary tangles, gliosis and
CC   neuronal loss. Hu-Asp1 protease substrate is useful for assaying
CC   hu-Asp1 proteolytic activity, by contacting hu-Asp1 protein with
CC   the substrate under acidic conditions and determining the level of
CC   hu-Asp1 proteolytic activity. The present sequence is wild-type
CC   human amyloid precursor protein (APP) beta-secretase specific
CC   substrate peptide, PHA-95812E. This peptide is used for assaying
CC   the beta-secretase activity of human Aspartyl protease 2a (Asp2a)
CC   protein. The peptide is also used for determining the relationship
CC   between Aspartyl protease 1 (Asp1) and APP protein.
XX
SQ   Sequence   10 AA;

     Query Match   100.0%; Score 49; DB 22; Length 10;
     Best Local Similarity   100.0%; Pred. No. 0.00059;
     Matches   10; Conservative   0; Mismatches   0; Indels   0; Gaps   0;

Qy   1 SEVKMDAEFR 10
               ||||||||||
Db   1 SEVKMDAEFR 10

RESULT 4
AAE06899
ID   AAE06899 standard; peptide; 10 AA.
XX
AC   AAE06899;
XX
DT   23-OCT-2001   (first entry)
XX
DE   Human amyloid precursor protein wild-type beta-secretase peptide.
XX
KW   Human; aspartyl protease 2; Asp 2; beta-amyloid precursor protein; APP;
KW   beta-secretase; Alzheimer's disease; dementia; amyloid plaque; gliosis;
KW   neurofibrillary tangle; neuronal loss; amyloid-beta peptide; nootropic;
KW   neuroprotective; antisense therapy; gene therapy.
XX
OS   Homo sapiens.
XX
FH   Key   Location/Qualifiers
FT   Cleavage-site   5..6
XX
PN   WO200150829-A2.
XX
PD   19-JUL-2001.
XX
PF   09-MAY-2001; 2001WO-IB00799.
XX
PR   09-MAY-2001; 2001WO-IB00799.
XX
PA   (BIEN/) BIENKOWSKI M J.
PA   (GURN/) GURNEY M E.
PA   (HEIN/) HEINRIKSON R L.
PA   (PARO/) PARODI L A.

PA   (YANR/) YAN R.
XX
PI   Bienkowski MJ, Gurney ME, Heinrikson RL, Parodi LA, Yan R;
XX
DR   WPI; 2001-483072/52.
XX
PT   Novel purified polypeptide comprising fragment of mammalian aspartyl
PT   protease 2, lacking Asp2 transmembrane domain and retaining beta
PT   secretase activity of Asp2 useful for identifying inhibitors of Asp2
PT   activity -
XX
PS   Claim 127; Page 80; 185pp; English.
XX
CC   The invention relates to human aspartyl proteases (Hu-Asp), beta-amyloid
CC   precursor protein (APP) isoforms and their corresponding DNA molecules.
CC   Human aspartyl proteases can act as beta-secretase proteases useful for
CC   treating Alzheimer's disease. APP isoforms are useful for identifying
CC   modulators of amyloid-beta peptide production, for use in designing
CC   therapeutics for the treatment and prevention of Alzheimer's disease,
CC   dementia, formation of amyloid plaques, neurofibrillary tangles, gliosis
CC   and neuronal loss. APP isoforms are also used in methods for identifying
CC   inhibitors and modulators of human Asp2 activity. The invention relates
CC   to a method for identifying agents that modulate the activity of human
CC   aspartyl protease Asp2. Amyloid-beta peptides obtained from APP are used
CC   as a means to screen in cellular assays for the inhibitors of beta- and
CC   gamma- secretase. Hu-Asp DNA fragments are useful as probes or primers in
CC   polymerase chain reactions (PCR). The probes are useful for detecting
CC   Hu-Asp nucleic acids in in vitro assays and in Northern and Southern
CC   blots. The present sequence is human amyloid precursor protein (APP)
CC   wild type beta-secretase peptide used in beta-secretase assay.
XX
SQ   Sequence   10 AA;

     Query Match   100.0%; Score 49; DB 22; Length 10;
     Best Local Similarity   100.0%; Pred. No. 0.00059;
     Matches   10; Conservative   0; Mismatches   0; Indels   0; Gaps   0;

Qy   1 SEVKMDAEFR 10
               ||||||||||
Db   1 SEVKMDAEFR 10

RESULT 5
AAU06628
ID   AAU06628 standard; Peptide; 10 AA.
XX
AC   AAU06628;
XX
DT   24-OCT-2001 (first entry)
XX
DE   Asp2 recognition site from wild-type APP.
XX
KW   Aspartyl protease; Asp2; beta-secretase; nootropic;
KW   neuroprotective; amyloid protein precursor; APP; Alzheimer's disease;
KW   amyloid-beta; Abeta.
XX
OS   Homo sapiens.

XX
FH   Key   Location/Qualifiers
FT   Cleavage-site   5
FT   /label= Asp2_protease_cleavage_site
XX
PN   WO200149098-A2.
XX
PD   12-JUL-2001.
XX
PF   09-MAY-2001; 2001WO-IB00798.
XX
PR   09-MAY-2001; 2001WO-IB00798.
XX
PA   (BIEN/) BIENKOWSKI M J.
PA   (GURN/) GURNEY M E.
PA   (HEIN/) HEINRIKSON R L.
PA   (PARO/) PARODI L A.
PA   (YANR/) YAN R.
XX
PI   Bienkowski MJ, Gurney ME, Heinrikson RL, Parodi LA, Yan R;
XX
DR   WPI; 2001-502549/55.
XX
PT   Novel purified polypeptide comprising fragment of mammalian aspartyl
PT   protease 2, lacking Asp2 transmembrane domain and retaining beta
PT   secretase activity of Asp2 useful for identifying inhibitors of Asp2
PT   activity -
XX
PS   Claim 127; Page 101; 185pp; English.
XX
CC   The invention relates to a purified polypeptide comprising a fragment of
CC   mammalian aspartyl protease (Asp)2 protein which lacks the Asp2
CC   transmembrane domain and the Asp2 protein, and where the polypeptide and
CC   the fragment retain the beta-secretase activity of the mammalian Asp2
CC   protein. The invention also details polynucleotides for the Asp
CC   proteins and vectors expressing them, and a polypeptide (isoform of
CC   amyloid protein precursor (APP)) comprising the amino acid sequence of an
CC   APP or its fragment containing an APP cleavage site recognizable by a
CC   mammalian beta-secretase, and further comprising two lysine residues at
CC   the carboxyl terminus of the amino acid sequence of the mammalian APP or
CC   APP fragment. Also included in the invention are methods of identifying
CC   modulators or inhibitors of Asp2. Modulators and inhibitors of Asp2 are
CC   useful for treating Alzheimer's disease. APP is useful in methods for
CC   identifying inhibitors or modulators of human Asp2 activity and
CC   amyloid-beta (Abeta) peptide production. APP is also useful in designing
CC   therapeutics for the treatment or prevention of Alzheimer's disease.
CC   APP comprising the APP-Sw-beta-secretase peptide sequence (NLDA), which
CC   is associated with increased levels of Abeta processing is useful in
CC   assays relating the Alzheimer's research. The expression vector is useful
CC   for recombinantly expressing APP. Nucleic acids that hybridise to
CC   Asp oligonucleotides are useful as probes or primers. The probes are
CC   useful for detecting Hu-Asp nucleic acids in in vitro assays and in
CC   Northern and Southern blots. The present sequence is a peptide substrate
CC   for Asp2 corresponding to the wild-type APP beta-secretase site.
XX
SQ   Sequence   10 AA;

```
Query Match            100.0%;  Score 49;  DB 22;  Length 10;
Best Local Similarity  100.0%;  Pred. No. 0.00059;
Matches   10;  Conservative   0;  Mismatches   0;  Indels   0;  Gaps   0;

Qy         1 SEVKMDAEFR 10
             ||||||||||
Db         1 SEVKMDAEFR 10


RESULT 6
AAU07227
ID    AAU07227 standard; Peptide; 10 AA.
XX
AC    AAU07227;
XX
DT    24-OCT-2001   (first entry)
XX
DE    Human beta-amyloid protein precursor, APP-beta40 and 42 secretase site.
XX
KW    Human; aspartyl protease 1; Asp-1; nootropic; neuroprotective;
KW    aspartyl protease 2; Asp2; amyloid protein precursor; APP;
KW    beta-secretase; Alzheimer's disease; APP-beta40; APP-beta42.
XX
OS    Homo sapiens.
XX
PN    WO200149097-A2.
XX
PD    12-JUL-2001.
XX
PF    09-MAY-2001; 2001WO-IB00797.
XX
PR    09-MAY-2001; 2001WO-IB00797.
XX
PA    (BIEN/) BIENKOWSKI M J.
PA    (GURN/) GURNEY M E.
PA    (HEIN/) HEINRIKSON R L.
PA    (PARO/) PARODI L A.
PA    (YANR/) YAN R.
XX
PI    Bienkowski MJ,  Gurney ME,  Heinrikson RL,  Parodi LA,  Yan R;
XX
DR    WPI; 2001-502548/55.
XX
PT    Novel purified polypeptide comprising fragment of mammalian aspartyl
PT    protease 2, lacking Asp2 transmembrane domain and retaining beta
PT    secretase activity of Asp2 useful for identifying inhibitors of Asp2
PT    activity  -
XX
PS    Claim 127; Page 101; 185pp; English.
XX
CC    The invention relates to a novel purified polypeptide comprising a
CC    fragment of mammalian aspartyl protease 2 (Asp2) protein which lacks the
CC    Asp2 transmembrane domain and the Asp2 protein, and where the polypeptide
CC    and the fragment retain the beta-secretase activity of the mammalian Asp2
CC    protein. Also included is an isoform of amyloid protein precursor (APP)
CC    comprising the amino acid sequence of a APP or its fragment containing
CC    an APP cleavage site recognisable by a mammalian beta-secretase, and
```

```
CC    further comprising two lysine residues at the carboxyl terminus of the
CC    amino acid sequence of the mammalian APP or APP fragment. The
CC    polypeptides are used for assaying for modulators of beta-secretase
CC    activity; identifying agents that inhibit the APP processing activity
CC    of human Asp2 aspartyl protease (Hu-Asp2); identifying agents that
CC    modulate the activity of Asp2; and for reducing cellular production of
CC    amyloid beta (Abeta) from APP. Agents identified by the above methods
CC    are useful for treating Alzheimer's disease; and for identifying
CC    modulators of amyloid-beta (Abeta) peptide production, for use in
CC    designing therapeutics for the treatment or prevention of Alzheimer's
CC    disease. Probes and primers derived from Asp nucleic acid sequences
CC    are useful for detecting Hu-Asp nucleic acids in in vitro assays and in
CC    Northern and Southern blots. The present sequence represents the
CC    amino acid sequence of human amyloid protein precursor, APP-beta40
CC    and APP-beta42 secretase sites.
XX
SQ    Sequence    10 AA;

      Query Match                100.0%;   Score 49;   DB 22;   Length 10;
      Best Local Similarity      100.0%;   Pred. No. 0.00059;
      Matches    10;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;


Qy          1 SEVKMDAEFR 10
              ||||||||||
Db          1 SEVKMDAEFR 10


RESULT 7
AAE02606
ID    AAE02606 standard; peptide; 10 AA.
XX
AC    AAE02606;
XX
DT    10-AUG-2001   (first entry)
XX
DE    Human wild-type APP beta-secretase substrate peptide, PHA-95812E.
XX
KW    Human; alpha-secretase; amyloid precursor protein; APP; therapy;
KW    Alzheimer's disease; antialzheimer's; aspartyl protease 2a; Asp2a;
KW    beta-secretase.
XX
OS    Homo sapiens.
XX
FH    Key             Location/Qualifiers
FT    Cleavage-site   5..6
XX
PN    WO200123533-A2.
XX
PD    05-APR-2001.
XX
PF    22-SEP-2000; 2000WO-US26080.
XX
PR    23-SEP-1999;   99US-0155493.
PR    23-SEP-1999;   99WO-US20881.
PR    13-OCT-1999;   99US-0416901.
PR    06-DEC-1999;   99US-0169232.
XX
```

```
PA    (PHAA ) PHARMACIA & UPJOHN CO.
XX
PI    Gurney M,  Bienkowski MJ;
XX
DR    WPI; 2001-290516/30.
XX
PT    Enzymes that cleave the alpha-secretase site of the amyloid precursor
PT    protein, useful for the treatment of Alzheimer's disease -
XX
PS    Example 12; Page 85; 189pp; English.
XX
CC    The present invention relates to enzymes for cleaving the alpha-
CC    secretase site of the amyloid precursor protein (APP) and methods of
CC    identifying those enzymes. The methods may be used to identify enzymes
CC    that may be used to cleave the alpha-secretase cleavage site of the APP
CC    protein. The enzymes may be used to treat or modulate the progress of
CC    Alzheimer's disease. The present sequence is human wild-type amyloid
CC    precursor protein (APP) beta-secretase specific substrate peptide,
CC    PHA-95812E. This peptide is used for assaying the beta-secretase activity
CC    of human Aspartyl protease 2a (Asp2a) protein. The peptide is also used
CC    for determining the relationship between Aspartyl protease 1 (Asp1) and
CC    APP protein.
XX
SQ    Sequence   10 AA;

   Query Match              100.0%;  Score 49;  DB 22;  Length 10;
   Best Local Similarity    100.0%;  Pred. No. 0.00059;
   Matches   10;  Conservative   0;  Mismatches   0;  Indels   0;  Gaps   0;

Qy        1 SEVKMDAEFR 10
            ||||||||||
Db        1 SEVKMDAEFR 10


RESULT 8
AAB66574
ID    AAB66574 standard; Peptide; 10 AA.
XX
AC    AAB66574;
XX
DT    12-APR-2001   (first entry)
XX
DE    Synthetic peptide derived from APP beta-secretase site.
XX
KW    Memapsin 2; nootropic; neuroprotective; amyloid precursor protein;
KW    APP; memapsin 2 inhibitor; Alzheimer's disease.
XX
OS    Synthetic.
XX
PN    WO200100665-A2.
XX
PD    04-JAN-2001.
XX
PF    27-JUN-2000; 2000WO-US17742.
XX
PR    28-JUN-1999;    99US-0141363.
PR    30-NOV-1999;    99US-0168060.
```

    Query Match   100.0%; Score 49; DB 22; Length 10;
    Best Local Similarity   100.0%; Pred. No. 0.00059;
    Matches   10; Conservative   0; Mismatches   0; Indels   0; Gaps   0;

Qy   1 SEVKMDAEFR 10
             ||||||||||
Db   1 SEVKMDAEFR 10

PT   Preventing or treating a disease associated with amyloid deposits,
PT   especially Alzheimer's disease, comprises administering amyloid
PT   specific antibody -
XX
PS   Disclosure; Figure 19; 143pp; English.
XX
CC   This invention describes a novel method of preventing or treating a
CC   disease associated with amyloid deposits of amyloid precursor protein
CC   (APP) Abeta fragments in the brain of a patient, which comprises
CC   administering to the patient: (a) an antibody that binds to Abeta, the
CC   antibody binds to an amyloid deposit and induces a clearing response (Fc
CC   receptor mediated phagocytosis) against it (b) a polypeptide containing
CC   an N-terminal segment of at least residues 1-5 of Abeta; or (c) an agent
CC   that induces an immunogenic response against residues 1-3 to 7-11 of
CC   Abeta. The products of the invention have nootropic and neuroprotective
CC   activity. The method is also useful for monitoring a course of treatment
CC   being administered to a patient e.g. active and passive immunization. The
CC   methods are useful for prophylactic and therapeutic treatment of
CC   Alzheimer's disease.
XX
SQ   Sequence   10 AA;

      Query Match   100.0%;   Score 49;   DB 22;   Length 10;
      Best Local Similarity   100.0%;   Pred. No. 0.00059;
      Matches   10;   Conservative   0;   Mismatches   0;   Indels   0;   Gaps   0;

Qy   1 SEVKMDAEFR 10
                | | | | | | | | | |
Db   1 SEVKMDAEFR 10

RESULT 10
AAB61336
ID   AAB61336 standard; peptide; 10 AA.
XX
AC   AAB61336;
XX
DT   02-APR-2001 (first entry)
XX
DE   Sythetic peptide from beta amyloid precursor protein.
XX
KW   Memapsin 2; catalyst; Alzheimer's.
XX
OS   Unidentified.
XX

PT   Purified recombinant catalytically active memapsin 2, used to screen
PT   inhibitors of it, which are used to treat and prevent Alzheimer's
PT   disease -

XX

PS   Claim 6; Page 11; 86pp; English.

XX

CC   The present invention relates to a purified recombinant
CC   catalytically active memapsin 2. The invention may be used for
CC   isolating inhibitors which are used to treat or prevent
CC   Alzheimer's disease. The invention may also be used to screen
CC   for individuals more genetically prone to develop Alzheimer's
CC   disease.

XX

SQ   Sequence   10 AA;

   Query Match   100.0%; Score 49; DB 22; Length 10;
   Best Local Similarity   100.0%; Pred. No. 0.00059;
   Matches   10; Conservative   0; Mismatches   0; Indels   0; Gaps   0;

Qy   1 SEVKMDAEFR 10
              | | | | | | | | | |
Db   1 SEVKMDAEFR 10

RESULT 11
ABG78375
ID   ABG78375 standard; Peptide; 10 AA.

XX

AC   ABG78375;

XX

DT   15-NOV-2002   (first entry)

XX

DE   Human beta amyloid precursor protein beta secretase site #1.

XX

KW   Human; memapsin 2; aspartic protease; beta secretase;
KW   degenerative disease; Alzheimer's disease; amyloid precursor protein;
KW   APP; neuroprotective; nootropic; inhibitor; cleavage site;
KW   substrate side-chain preference.

XX

```
OS    Homo sapiens.
XX
PN    WO200253594-A2.
XX
PD    11-JUL-2002.
XX
PF    28-DEC-2001; 2001WO-US50826.
XX
PR    28-DEC-2000; 2000US-258705P.
PR    14-MAR-2001; 2001US-275756P.
XX
PA    (OKLA-) OKLAHOMA MEDICAL RES FOUND.
PA    (UNII ) UNIV ILLINOIS FOUND.
XX
PI    Tang JJN,  Koelsch G,  Ghosh AK;
XX
DR    WPI; 2002-619088/66.
XX
PT    New memapsin 2 activity inhibitor useful in treatment of e.g.
PT    Alzheimer's disease  -
XX
PS    Disclosure; Page 23; 74pp; English.
XX
CC    The invention relates to an inhibitor of catalytically active memapsin 2
CC    (an aspartic protease which can cleave at beta secretase sites), which
CC    binds to the active site of memapsin 2 defined by the presence of two
CC    catalytic aspartic residues and substrate binding cleft. Also
CC    included is a method of determination of the substrate side-chain
CC    preference in memapsin 2 sub-sites comprising: (a) reacting a mixture of
CC    memapsin 2 substrates with memapsin 2, and determining the sub-site
CC    preference of memapsin 2 by determining relative initial hydrolysis rates
CC    of the mixture of memapsin 2 substrates; or (b) preparing a combinatorial
CC    library of memapsin 2 inhibitors containing a base sequence taken from
CC    OM99-2 (Glu-Val-Asn-Leu-Ala-Ala-Glu-phe), probing the library of
CC    inhibitors with memapsin 2 which binds to several inhibitors to generate
CC    several bound memapsin 2, and detecting the bound memapsin 2 with an
CC    antibody raised to memapsin 2 and an alkaline phosphatase conjugated
CC    secondary antibody. The inhibitors may be used in the manufacture of a
CC    medicament for the treatment of Alzheimer's disease since memapsin 2 may
CC    be involved in the cleavage of amyloid precursor protein (APP), and for
CC    determining the substrate side-chain preference in memapsin 2 sub-sites.
CC    The present sequence represents a beta secretase cleavage site used
CC    to determine the substrate specificity of human memapsin 2.
XX
SQ    Sequence   10 AA;

   Query Match             100.0%;  Score 49;  DB 23;  Length 10;
   Best Local Similarity   100.0%;  Pred. No. 0.00059;
   Matches    10;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy            1 SEVKMDAEFR 10
                ||||||||||
Db            1 SEVKMDAEFR 10


RESULT 12
ABG30940
```

```
CC   manufacturing a medicament for the treatment or prevention of disorders
CC   responsive to the modulation of Nogo activity, in alleviating the
CC   symptoms or improving the condition of a patient suffering from this
CC   disorder, in axon regeneration, or in preventing metastasis or spreading
CC   of a cancer. The polynucleotide may also be an essential component in
CC   assays, a probe, in recombinant protein synthesis, and in gene therapy
CC   techniques. The present amino acid sequence represents a cleavage peptide
CC   that was used in the methods of the invention.
XX
SQ   Sequence   10 AA;

   Query Match              100.0%;   Score 49;   DB 23;   Length 10;
   Best Local Similarity    100.0%;   Pred. No. 0.00059;
   Matches   10;  Conservative   0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy        1 SEVKMDAEFR 10
            ||||||||||
Db        1 SEVKMDAEFR 10


RESULT 13
AAU99490
ID   AAU99490 standard; peptide; 10 AA.
XX
AC   AAU99490;
XX
DT   07-OCT-2002   (first entry)
XX
DE   Peptide #1 used as substrate for human memapsin 2.
XX
KW   Human; memapsin 2; beta secretase; aspartic protease; APP;
KW   beta-amyloid precursor protein; amyloid plaque; Alzheimer's disease;
KW   neuroprotective; nootropic.
XX
OS   Homo sapiens.
OS   Synthetic.
XX
PN   US2002049303-A1.
XX
PD   25-APR-2002.
XX
PF   28-FEB-2001; 2001US-0796264.
XX
PR   28-JUN-1999;    99US-141363P.
PR   30-NOV-1999;    99US-168060P.
PR   25-JAN-2000;  2000US-177836P.
PR   27-JAN-2000;  2000US-178368P.
PR   27-JUN-2000;  2000US-0604608.
XX
PA   (TANG/) TANG J J N.
PA   (LINX/) LIN X.
PA   (KOEL/) KOELSCH G.
PA   (HONG/) HONG L.
XX
PI   Tang JJN, Lin X, Koelsch G, Hong L;
XX
DR   WPI; 2002-507280/54.
```

CC   The present invention relates to methods for the production of
CC   purified, recombinant catalytically active, memapsin 2 (beta
CC   secretase). Memapsin 2, a member of the aspartic protease family,
CC   cleaves beta-amyloid precursor protein (APP) found in amyloid plaques.
CC   The recombinant memapsin 2 is useful for identifying inhibitors of
CC   memapsin 2 in the design of drugs for the treatment and/or prevention
CC   of Alzheimer's disease. The recombinant memapsin 2 can be used to
CC   immunise against Alzheimer's disease. The present sequence represents
CC   a peptide used as a substrate for human memapsin 2.
XX
SQ   Sequence   10 AA;

     Query Match   100.0%; Score 49; DB 23; Length 10;
     Best Local Similarity   100.0%; Pred. No. 0.00059;
     Matches   10; Conservative   0; Mismatches   0; Indels   0; Gaps   0;

Qy   1 SEVKMDAEFR 10
             ||||||||||
Db   1 SEVKMDAEFR 10

RESULT 14
ABB78615

```
XX
PI     Bienkowkski MJ,   Gurney M;
XX
DR     WPI; 2002-396337/43.
XX
PT     Human aspartyl protease 1 substrates useful in assays to detect
PT     aspartyl protease activity, e.g. for the diagnosis of Alzheimer's
PT     disease -
XX
PS     Example 15; Page 92; 182pp; English.
XX
CC     The present invention describes a human aspartyl protease 1 (hu-Asp1)
CC     substrate (I) which comprises a peptide of no more than 50 amino acids,
CC     and which comprises the 8 amino acid sequence Gly-Leu-Ala-Leu-Ala-Leu-
CC     Glu-Pro. Also described are: (1) a method (II) for assaying hu-Asp1
CC     proteolytic activity, comprising: (a) contacting a hu-Asp1 protein with
CC     (I) under acidic conditions; and (b) determining the level of hu-Asp1
CC     proteolytic activity; (2) a purified polynucleotide (III) comprising a
CC     nucleotide sequence that hybridises under stringent conditions to the
CC     non-coding strand complementary to a defined 1804 nucleotide sequence
CC     (see ABL52456) where the nucleotide sequence encodes a polypeptide having
CC     Asp1 proteolytic activity and lacks nucleotides encoding a transmembrane
CC     domain); (3) a purified polynucleotide (III') comprising a sequence that
CC     hybridises under stringent conditions to (III) (the nucleotide sequence
CC     encodes a polypeptide further lacking a pro-peptide domain corresponding
CC     to amino acids 23-62 of hu-Asp1 (see ABB78589)); (4) a vector (IV)
CC     comprising (III) or (III'); and (5) a host cell (V) transformed or
CC     transfected with (III), (III') and/or (IV). The hu-Asp1 protease
CC     substrate (I) may be used as an enzyme substrate in assays to detect
CC     aspartyl protease activity, (II) and therefore diagnose diseases
CC     associated with aberrant hu-Asp1 expression and activity such as
CC     Alzheimer's disease. Hu-Asp1 has been localised to chromosome 21, while
CC     hu-Asp2 has been localised to chromosome 11q23.3-24.1. The present
CC     sequence represents a beta-secretase specific substrate peptide which is
CC     used in an example from the present invention.
XX
SQ     Sequence    10 AA;

   Query Match             100.0%;   Score 49;   DB 23;   Length 10;
   Best Local Similarity   100.0%;   Pred. No. 0.00059;
   Matches    10;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy           1 SEVKMDAEFR 10
               ||||||||||
Db           1 SEVKMDAEFR 10


RESULT 15
ABB06426
ID     ABB06426 standard; Peptide; 10 AA.
XX
AC     ABB06426;
XX
DT     31-MAY-2002   (first entry)
XX
DE     Human APP beta-secretase cleavage sequence SEQ ID NO:20.
XX
```

      Query Match   100.0%; Score 49; DB 23; Length 10;
      Best Local Similarity   100.0%; Pred. No. 0.00059;
      Matches   10; Conservative   0; Mismatches   0; Indels   0; Gaps   0;

Qy   1 SEVKMDAEFR 10
              | | | | | | | | | |
Db   1 SEVKMDAEFR 10

Search completed: January 21, 2004, 09:22:25
Job time : 3.63862 secs

GenCore version 5.1.6
Copyright (c) 1993 - 2004 Compugen Ltd.

OM protein - protein search, using sw model

Run on: January 21, 2004, 09:19:55 ; Search time 0.898662 Seconds
                                             (without alignments)
                                             470.821 Million cell updates/sec

Title: US-09-869-414A-64
Perfect score: 49
Sequence: 1 SEVKMDAEFR 10

Scoring table: BLOSUM62
                Gapop 10.0 , Gapext 0.5

Searched: 328717 seqs, 42310858 residues

Total number of hits satisfying chosen parameters: 328717

Minimum DB seq length: 0
Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%
                 Maximum Match 100%
                 Listing first 45 summaries

Database :   Issued_Patents_AA:*
                1:   /cgn2_6/ptodata/1/iaa/5A_COMB.pep:*
                2:   /cgn2_6/ptodata/1/iaa/5B_COMB.pep:*
                3:   /cgn2_6/ptodata/1/iaa/6A_COMB.pep:*
                4:   /cgn2_6/ptodata/1/iaa/6B_COMB.pep:*
                5:   /cgn2_6/ptodata/1/iaa/PCTUS_COMB.pep:*
                6:   /cgn2_6/ptodata/1/iaa/backfiles1.pep:*

        Pred. No. is the number of results predicted by chance to have a
        score greater than or equal to the score of the result being printed,
        and is derived by analysis of the total score distribution.

                               SUMMARIES
                    %
Result   Query
  No.   Score   Match Length DB   ID   Description
----
     1   49   100.0   10   4 US-09-548-372D-64   Sequence 64, Appl
     2   49   100.0   10   4 US-09-548-367D-64   Sequence 64, Appl
     3   49   100.0   10   4 US-09-551-853D-64   Sequence 64, Appl
     4   49   100.0   10   4 US-09-604-608-4   Sequence 4, Appli
     5   49   100.0   11   5 PCT-US94-07043A-7   Sequence 7, Appli
     6   49   100.0   12   5 PCT-US94-07043A-2   Sequence 2, Appli
     7   49   100.0   16   5 PCT-US94-07043A-1   Sequence 1, Appli
     8   49   100.0   27   1 US-08-141-324-11   Sequence 11, Appl
     9   49   100.0   27   1 US-08-541-902-11   Sequence 11, Appl
    10   49   100.0   45   1 US-08-462-859A-5   Sequence 5, Appli
    11   49   100.0   45   1 US-08-123-659A-5   Sequence 5, Appli

```
12     49   100.0     45   1   US-08-464-247A-5        Sequence 5, Appli
13     49   100.0     45   1   US-08-464-248A-5        Sequence 5, Appli
14     49   100.0     58   1   US-08-371-930-25        Sequence 25, Appl
15     49   100.0     58   5   PCT-US94-01712-25       Sequence 25, Appl
16     49   100.0     63   1   US-08-462-859A-3        Sequence 3, Appli
17     49   100.0     63   1   US-08-462-859A-4        Sequence 4, Appli
18     49   100.0     63   1   US-08-123-659A-3        Sequence 3, Appli
19     49   100.0     63   1   US-08-123-659A-4        Sequence 4, Appli
20     49   100.0     63   1   US-08-464-247A-3        Sequence 3, Appli
21     49   100.0     63   1   US-08-464-247A-4        Sequence 4, Appli
22     49   100.0     63   1   US-08-464-248A-3        Sequence 3, Appli
23     49   100.0     63   1   US-08-464-248A-4        Sequence 4, Appli
24     49   100.0    105   2   US-08-729-345-1         Sequence 1, Appli
25     49   100.0    117   2   US-08-729-345-3         Sequence 3, Appli
26     49   100.0    152   6   5187153-4               Patent No. 5187153
27     49   100.0    162   6   5220013-4               Patent No. 5220013
28     49   100.0    162   6   5223482-4               Patent No. 5223482
29     49   100.0    264   1   US-07-990-893-5         Sequence 5, Appli
30     49   100.0    487   1   US-08-462-859A-9        Sequence 9, Appli
31     49   100.0    487   1   US-08-123-659A-9        Sequence 9, Appli
32     49   100.0    487   1   US-08-464-247A-9        Sequence 9, Appli
33     49   100.0    487   1   US-08-464-248A-9        Sequence 9, Appli
34     49   100.0    492   1   US-08-462-859A-7        Sequence 7, Appli
35     49   100.0    492   1   US-08-123-659A-7        Sequence 7, Appli
36     49   100.0    492   1   US-08-464-247A-7        Sequence 7, Appli
37     49   100.0    492   1   US-08-464-248A-7        Sequence 7, Appli
38     49   100.0    537   1   US-08-453-552-4         Sequence 4, Appli
39     49   100.0    537   2   US-08-710-637-4         Sequence 4, Appli
40     49   100.0    537   5   PCT-US93-00907-4        Sequence 4, Appli
41     49   100.0    656   1   US-08-371-930-23        Sequence 23, Appl
42     49   100.0    656   5   PCT-US94-01712-23       Sequence 23, Appl
43     49   100.0    676   1   US-08-371-930-24        Sequence 24, Appl
44     49   100.0    676   5   PCT-US94-01712-24       Sequence 24, Appl
45     49   100.0    694   1   US-08-339-152A-18       Sequence 18, Appl
```

ALIGNMENTS

RESULT 1
US-09-548-372D-64
; Sequence 64, Application US/09548372D
; Patent No. 6420534
; GENERAL INFORMATION:
;   APPLICANT: GURNEY ET AL.
;   TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR
AND USES
;   TITLE OF INVENTION: THEREOF
;   FILE REFERENCE: 29915/6280I
;   CURRENT APPLICATION NUMBER: US/09/548,372D
;   CURRENT FILING DATE: 2000-04-12
;   PRIOR APPLICATION NUMBER: US 60/155,493
;   PRIOR FILING DATE: 1999-09-23
;   PRIOR APPLICATION NUMBER: US 09/404,133
;   PRIOR FILING DATE: 1999-09-23
;   PRIOR APPLICATION NUMBER: PCT/US99/20881
;   PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: US 60/101,594
; PRIOR FILING DATE: 1998-09-24
; NUMBER OF SEQ ID NOS: 73
; SOFTWARE: PatentIn version 3.1
; SEQ ID NO 64
; LENGTH: 10
; TYPE: PRT
; ORGANISM: Artificial sequence
; FEATURE:
; OTHER INFORMATION: Synthetic peptide
US-09-548-372D-64

    Query Match   100.0%; Score 49; DB 4; Length 10;
    Best Local Similarity 100.0%; Pred. No. 0.00061;
    Matches   10; Conservative   0; Mismatches   0; Indels   0; Gaps   0;

Qy   1 SEVKMDAEFR 10
             ||||||||||
Db   1 SEVKMDAEFR 10

RESULT 2
US-09-548-367D-64
; Sequence 64, Application US/09548367D
; Patent No. 6440698
; GENERAL INFORMATION:
; APPLICANT: GURNEY ET AL.
; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR
AND USES
; TITLE OF INVENTION: THEREOF
; FILE REFERENCE: 29915/6280H
; CURRENT APPLICATION NUMBER: US/09/548,367D
; CURRENT FILING DATE: 2000-04-12
; PRIOR APPLICATION NUMBER: US 60/155,493
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: US 09/404,133
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: PCT/US99/20881
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: US 60/101,594
; PRIOR FILING DATE: 1998-09-24
; NUMBER OF SEQ ID NOS: 73
; SOFTWARE: PatentIn version 3.1
; SEQ ID NO 64
; LENGTH: 10
; TYPE: PRT
; ORGANISM: Artificial sequence
; FEATURE:
; OTHER INFORMATION: Synthetic peptide
US-09-548-367D-64

    Query Match   100.0%; Score 49; DB 4; Length 10;
    Best Local Similarity 100.0%; Pred. No. 0.00061;
    Matches   10; Conservative   0; Mismatches   0; Indels   0; Gaps   0;

Qy   1 SEVKMDAEFR 10
             ||||||||||

RESULT 3
US-09-551-853D-64
; Sequence 64, Application US/09551853D
; Patent No. 6500667
; GENERAL INFORMATION:
;   APPLICANT: GURNEY ET AL.
;   TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR
AND USES
;   TITLE OF INVENTION: THEREOF
;   FILE REFERENCE: 29915/6280L
;   CURRENT APPLICATION NUMBER: US/09/551,853D
;   CURRENT FILING DATE: 2000-04-18
;   PRIOR APPLICATION NUMBER: US 60/155,493
;   PRIOR FILING DATE: 1999-09-23
;   PRIOR APPLICATION NUMBER: US 09/404,133
;   PRIOR FILING DATE: 1999-09-23
;   PRIOR APPLICATION NUMBER: PCT/US99/20881
;   PRIOR FILING DATE: 1999-09-23
;   PRIOR APPLICATION NUMBER: US 60/101,594
;   PRIOR FILING DATE: 1998-09-24
;   NUMBER OF SEQ ID NOS: 73
;   SOFTWARE: PatentIn version 3.1
; SEQ ID NO 64
;   LENGTH: 10
;   TYPE: PRT
;   ORGANISM: Artificial sequence
;   FEATURE:
;   OTHER INFORMATION: Synthetic peptide
US-09-551-853D-64

    Query Match   100.0%; Score 49; DB 4; Length 10;
    Best Local Similarity 100.0%; Pred. No. 0.00061;
    Matches   10; Conservative   0; Mismatches   0; Indels   0; Gaps   0;

Qy   1 SEVKMDAEFR 10
              ||||||||||
Db   1 SEVKMDAEFR 10

RESULT 4
US-09-604-608-4
; Sequence 4, Application US/09604608
; Patent No. 6545127
; GENERAL INFORMATION:
;   APPLICANT: Tang, Jordan J.N.
;   APPLICANT: Lin, Xinli
;   APPLICANT: Koelsch, Gerald
;   TITLE OF INVENTION: Catalytically Active Recombinant Memapsin and Methods
;   TITLE OF INVENTION: of Use Thereof
;   FILE REFERENCE: OMRF 179
;   CURRENT APPLICATION NUMBER: US/09/604,608
;   CURRENT FILING DATE: 2000-06-27
;   PRIOR APPLICATION NUMBER: 60/141,363
;   PRIOR FILING DATE: 1999-06-28

;   PRIOR APPLICATION NUMBER: 60/168,060
;   PRIOR FILING DATE: 1999-11-30
;   PRIOR APPLICATION NUMBER: 60/177,836
;   PRIOR FILING DATE: 2000-01-25
;   PRIOR APPLICATION NUMBER: 60/178,368
;   PRIOR FILING DATE: 2000-01-27
;   PRIOR APPLICATION NUMBER: 60/210,292
;   PRIOR FILING DATE: 2000-06-08
;   NUMBER OF SEQ ID NOS: 31
;   SOFTWARE: PatentIn Ver. 2.1
; SEQ ID NO 4
;   LENGTH: 10
;   TYPE: PRT
;   ORGANISM: Artificial Sequence
;   FEATURE:
;   OTHER INFORMATION: Description of Artificial Sequence: Primer
US-09-604-608-4

  Query Match   100.0%; Score 49; DB 4; Length 10;
  Best Local Similarity   100.0%; Pred. No. 0.00061;
  Matches   10; Conservative   0; Mismatches   0; Indels   0; Gaps   0;

Qy   1 SEVKMDAEFR 10
            ||||||||||
Db   1 SEVKMDAEFR 10

RESULT 5
PCT-US94-07043A-7
; Sequence 7, Application PC/TUS9407043A
;   GENERAL INFORMATION:
;   APPLICANT: Tamburini, Paul P.; Benz, G nter; H bich,
;   APPLICANT: Dieter; Dreyer, Robert N.; Koenig, Gerhard
;   TITLE OF INVENTION: CATHEPSIN D IS AN AMYLOIDOGENIC
;   TITLE OF INVENTION: PROTEASE IN ALZHEIMER S DISEASE
;   NUMBER OF SEQUENCES: 11
;   CORRESPONDENCE ADDRESS:
;   ADDRESSEE: Miles Inc.
;   STREET: 400 Morgan Lane
;   CITY: West Haven
;   STATE: Connecticut
;   COUNTRY: USA
;   ZIP: 06516
;   COMPUTER READABLE FORM:
;   MEDIUM TYPE: Diskette, 3.50 inch, 800 kb storage
;   COMPUTER: Sharp PC 4600
;   OPERATING SYSTEM: MS-DOS
;   SOFTWARE: WordPerfect 5.1
;   CURRENT APPLICATION DATA:
;   APPLICATION NUMBER: PCT/US94/07043A
;   FILING DATE: June 21, 1994
;   CLASSIFICATION:
;   PRIOR APPLICATION DATA:
;   APPLICATION NUMBER: PCT/US93/10889
;   FILING DATE: November 12, 1993
;   PRIOR APPLICATION DATA:
;   APPLICATION NUMBER: 07/995,660

PCT-US94-07043A-7

  Query Match   100.0%; Score 49; DB 5; Length 11;
  Best Local Similarity   100.0%; Pred. No. 0.00067;
  Matches   10; Conservative   0; Mismatches   0; Indels   0; Gaps   0;

Qy   1 SEVKMDAEFR 10
            | | | | | | | | | |
Db   2 SEVKMDAEFR 11

RESULT 6
PCT-US94-07043A-2

```
  Query Match                100.0%;  Score 49;  DB 5;  Length 12;
  Best Local Similarity      100.0%;  Pred. No. 0.00073;
  Matches   10;  Conservative   0;  Mismatches   0;  Indels   0;  Gaps   0;


Qy        1 SEVKMDAEFR 10
            ||||||||||
Db        2 SEVKMDAEFR 11
```

Query Match   100.0%;   Score 49;   DB 5;   Length 16;
Best Local Similarity   100.0%;   Pred. No. 0.001;
Matches   10; Conservative   0; Mismatches   0; Indels   0; Gaps   0;

Qy   1 SEVKMDAEFR 10
            ||||||||||
Db   2 SEVKMDAEFR 11

RESULT 8
US-08-141-324-11
; Sequence 11, Application US/08141324
; Patent No. 5475097
; GENERAL INFORMATION:
;   APPLICANT: Travis, James
;   APPLICANT: Potempa, Jan S.
;   APPLICANT: Barr, Philip J.
;   APPLICANT: Pavloff, Nadine
;   APPLICANT: Pike, Robert N.
;   TITLE OF INVENTION: Lysine-specific Porphyromonas gingivalis
;   TITLE OF INVENTION: Protease
;   NUMBER OF SEQUENCES: 28
;   CORRESPONDENCE ADDRESS:
;   ADDRESSEE: Greenlee and Winner, P.C.
;   STREET: 5370 Manhattan Circle, Suite 201
;   CITY: Boulder
;   STATE: CO
;   COUNTRY: US
;   ZIP: 80303
;   COMPUTER READABLE FORM:
;   MEDIUM TYPE: Floppy disk
;   COMPUTER: IBM PC compatible
;   OPERATING SYSTEM: PC-DOS/MS-DOS
;   SOFTWARE: PatentIn Release #1.0, Version #1.25
;   CURRENT APPLICATION DATA:
;   APPLICATION NUMBER: US/08/141,324
;   FILING DATE: 21-OCT-1993
;   CLASSIFICATION: 424
;   ATTORNEY/AGENT INFORMATION:

; INFORMATION FOR SEQ ID NO: 11:
;   SEQUENCE CHARACTERISTICS:
;   LENGTH: 27 amino acids
;   TYPE: amino acid
;   STRANDEDNESS: single
;   TOPOLOGY: linear
;   MOLECULE TYPE: peptide
;   HYPOTHETICAL: NO
;   ANTI-SENSE: NO
US-08-141-324-11

   Query Match   100.0%; Score 49; DB 1; Length 27;
   Best Local Similarity   100.0%; Pred. No. 0.0017;
   Matches   10; Conservative   0; Mismatches   0; Indels   0; Gaps   0;

Qy   1 SEVKMDAEFR 10
              ||||||||||
Db   4 SEVKMDAEFR 13

RESULT 9
US-08-541-902-11
; Sequence 11, Application US/08541902
; Patent No. 5707620
; GENERAL INFORMATION:
;   APPLICANT: Travis, James
;   APPLICANT: Potempa, Jan S.
;   APPLICANT: Barr, Philip J.
;   APPLICANT: Pavloff, Nadine
;   APPLICANT: Pike, Robert N.
;   TITLE OF INVENTION: Lysine-specific Porphyromonas gingivalis
;   TITLE OF INVENTION: Protease
;   NUMBER OF SEQUENCES: 28
;   CORRESPONDENCE ADDRESS:
;   ADDRESSEE: Greenlee and Winner, P.C.
;   STREET: 5370 Manhattan Circle, Suite 201
;   CITY: Boulder
;   STATE: CO
;   COUNTRY: US
;   ZIP: 80303
;   COMPUTER READABLE FORM:
;   MEDIUM TYPE: Floppy disk
;   COMPUTER: IBM PC compatible
;   OPERATING SYSTEM: PC-DOS/MS-DOS
;   SOFTWARE: PatentIn Release #1.0, Version #1.25
;   CURRENT APPLICATION DATA:
;   APPLICATION NUMBER: US/08/541,902
;   FILING DATE:
;   CLASSIFICATION: 435
;   PRIOR APPLICATION DATA:
;   APPLICATION NUMBER: US/08/141,324

```
;       FILING DATE:  21-OCT-1993
;     ATTORNEY/AGENT INFORMATION:
;       NAME:  Ferber, Donna M.
;       REGISTRATION NUMBER:  33,878
;       REFERENCE/DOCKET NUMBER:  44-93
;     TELECOMMUNICATION INFORMATION:
;       TELEPHONE:  303-499-8080
;       TELEFAX:  303-499-8089
;   INFORMATION FOR SEQ ID NO:  11:
;     SEQUENCE CHARACTERISTICS:
;       LENGTH:  27 amino acids
;       TYPE:  amino acid
;       STRANDEDNESS:  single
;       TOPOLOGY:  linear
;     MOLECULE TYPE:  peptide
;     HYPOTHETICAL:  NO
;     ANTI-SENSE:  NO
US-08-541-902-11
```

```
   Query Match            100.0%;  Score 49;  DB 1;  Length 27;
   Best Local Similarity  100.0%;  Pred. No. 0.0017;
   Matches   10;  Conservative   0;  Mismatches   0;  Indels   0;  Gaps   0;


Qy        1 SEVKMDAEFR 10
            ||||||||||
Db        4 SEVKMDAEFR 13
```

```
RESULT 10
US-08-462-859A-5
; Sequence 5, Application US/08462859A
; Patent No. 5652092
;  GENERAL INFORMATION:
;     APPLICANT:  Jacobsen, J. S.
;     APPLICANT:  Vitek, M. P.
;     TITLE OF INVENTION:  No. 5652092el Amyloid Precursor and Method of
;     TITLE OF INVENTION:  Using Same to Access Agents Which Down-Regulate
Formation
;     TITLE OF INVENTION:  of B-Amyloid Peptide
;     NUMBER OF SEQUENCES:  19
;     CORRESPONDENCE ADDRESS:
;       ADDRESSEE:  American Cyanamid Company
;       STREET:  One Cyanamid Plaza
;       CITY:  Wayne
;       STATE:  New Jersey
;       COUNTRY:  United States
;       ZIP:  07470-8426
;     COMPUTER READABLE FORM:
;       MEDIUM TYPE:  Floppy disk
;       COMPUTER:  IBM PC compatible
;       OPERATING SYSTEM:  PC-DOS/MS-DOS
;       SOFTWARE:  PatentIn Release #1.0, Version #1.30
;     CURRENT APPLICATION DATA:
;       APPLICATION NUMBER:  US/08/462,859A
;       FILING DATE:  05-JUN-1995
;       CLASSIFICATION:  435
;     ATTORNEY/AGENT INFORMATION:
```

```
;       NAME:  Barnhard, Elizabeth M.
;       REGISTRATION NUMBER:  31,088
;       REFERENCE/DOCKET NUMBER:  31,844-04
;    TELECOMMUNICATION INFORMATION:
;       TELEPHONE:  (201)831-3246
;       TELEFAX:  (201)831-3305
;  INFORMATION FOR SEQ ID NO:  5:
;    SEQUENCE CHARACTERISTICS:
;       LENGTH:  45 amino acids
;       TYPE:  amino acid
;       STRANDEDNESS:
;       TOPOLOGY:  linear
;    MOLECULE TYPE:  protein
US-08-462-859A-5
```

```
  Query Match              100.0%;  Score 49;  DB 1;  Length 45;
  Best Local Similarity    100.0%;  Pred. No. 0.003;
  Matches   10;  Conservative   0;  Mismatches   0;  Indels   0;  Gaps   0;


Qy          1 SEVKMDAEFR 10
              ||||||||||
Db          5 SEVKMDAEFR 14
```

```
RESULT 11
US-08-123-659A-5
; Sequence 5, Application US/08123659A
; Patent No. 5656477
;  GENERAL INFORMATION:
;    APPLICANT:  Jacobsen, J. S.
;    APPLICANT:  Vitek, M. P.
;    TITLE OF INVENTION:  No. 5656477el Amyloid Precursor and Method of
;    TITLE OF INVENTION:  Using Same to Access Agents Which Down-Regulate
Formation
;    TITLE OF INVENTION:  of B-Amyloid Peptide
;    NUMBER OF SEQUENCES:  19
;    CORRESPONDENCE ADDRESS:
;      ADDRESSEE:  Anne Rosenblum
;      STREET:  163 Delaware Avenue, Suite 212
;      CITY:  Delmar
;      STATE:  New York
;      COUNTRY:  U.S.A.
;      ZIP:  12054
;    COMPUTER READABLE FORM:
;      MEDIUM TYPE:  Floppy disk
;      COMPUTER:  IBM PC compatible
;      OPERATING SYSTEM:  PC-DOS/MS-DOS
;      SOFTWARE:  PatentIn Release #1.0, Version #1.25
;    CURRENT APPLICATION DATA:
;      APPLICATION NUMBER:  US/08/123,659A
;      FILING DATE:  20-SEP-1993
;      CLASSIFICATION:  435
;    ATTORNEY/AGENT INFORMATION:
;      NAME:  Rosenblum, Anne M.
;      REGISTRATION NUMBER:  30,419
;      REFERENCE/DOCKET NUMBER:  31,844-01
;    TELECOMMUNICATION INFORMATION:
```

;   TELEPHONE: (518)475-0611
;   TELEFAX: (518)475-0619
; INFORMATION FOR SEQ ID NO: 5:
;   SEQUENCE CHARACTERISTICS:
;   LENGTH: 45 amino acids
;   TYPE: amino acid
;   TOPOLOGY: linear
;   MOLECULE TYPE: protein
US-08-123-659A-5

  Query Match   100.0%;   Score 49;   DB 1;   Length 45;
  Best Local Similarity   100.0%;   Pred. No. 0.003;
  Matches   10; Conservative   0;   Mismatches   0;   Indels   0;   Gaps   0;

Qy   1 SEVKMDAEFR 10
              ||||||||||
Db   5 SEVKMDAEFR 14

RESULT 12
US-08-464-247A-5
; Sequence 5, Application US/08464247A
; Patent No. 5693478
; GENERAL INFORMATION:
;   APPLICANT: Jacobsen, J. S.
;   APPLICANT: Vitek, M. P.
;   TITLE OF INVENTION: No. 5693478el Amyloid Precursor and Method of
;   TITLE OF INVENTION: Using Same to Access Agents Which Down-Regulate
Formation
;   TITLE OF INVENTION: of B-Amyloid Peptide
;   NUMBER OF SEQUENCES: 19
;   CORRESPONDENCE ADDRESS:
;   ADDRESSEE: American Cyanamid Company
;   STREET: One Campus Drive
;   CITY: Parsippany
;   STATE: New Jersey
;   COUNTRY: United States
;   ZIP: 07054
;   COMPUTER READABLE FORM:
;   MEDIUM TYPE: Floppy disk
;   COMPUTER: IBM PC compatible
;   OPERATING SYSTEM: PC-DOS/MS-DOS
;   SOFTWARE: PatentIn Release #1.0, Version #1.30
;   CURRENT APPLICATION DATA:
;   APPLICATION NUMBER: US/08/464,247A
;   FILING DATE: 05-JUN-1995
;   CLASSIFICATION: 435
;   ATTORNEY/AGENT INFORMATION:
;   NAME: Barnhard, Elizabeth M.
;   REGISTRATION NUMBER: 31,088
;   REFERENCE/DOCKET NUMBER: 31,844-03
;   TELECOMMUNICATION INFORMATION:
;   TELEPHONE: 201-683-2158
;   TELEFAX: 201-683-4117
; INFORMATION FOR SEQ ID NO: 5:
;   SEQUENCE CHARACTERISTICS:
;   LENGTH: 45 amino acids

GenCore version 5.1.6
Copyright (c) 1993 - 2004   Compugen Ltd.

OM protein - protein search, using sw model

Run on: January 21, 2004, 09:16:55 ; Search time 0.917782 Seconds
                                            (without alignments)
                                            1047.838 Million cell updates/sec

Title: US-09-869-414A-64
Perfect score: 49
Sequence: 1 SEVKMDAEFR 10

Scoring table: BLOSUM62
                Gapop 10.0 , Gapext 0.5

Searched: 283308 seqs, 96168682 residues

Total number of hits satisfying chosen parameters: 283308

Minimum DB seq length: 0
Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%
                 Maximum Match 100%
                 Listing first 45 summaries

Database :   PIR_76:*
                1: pir1:*
                2: pir2:*
                3: pir3:*
                4: pir4:*

        Pred. No. is the number of results predicted by chance to have a
        score greater than or equal to the score of the result being printed,
        and is derived by analysis of the total score distribution.

                              SUMMARIES
                       %
Result   Query
   No.   Score   Match Length DB   ID   Description
----
      1   49   100.0   57 2   E60045   Alzheimer's diseas
      2   49   100.0   57 2   F60045   Alzheimer's diseas
      3   49   100.0   57 2   G60045   Alzheimer's diseas
      4   49   100.0   57 2   D60045   Alzheimer's diseas
      5   49   100.0   57 2   A60045   Alzheimer's diseas
      6   49   100.0   57 2   B60045   Alzheimer's diseas
      7   49   100.0   82 2   PQ0438   Alzheimer's diseas
      8   49   100.0   695 1   A49795   Alzheimer's diseas
      9   49   100.0   770 1   QRHUA4   Alzheimer's diseas
     10   44   89.8   33 2   S23094   beta-amyloid prote
     11   44   89.8   695 2   A27485   Alzheimer's diseas
     12   44   89.8   695 2   S00550   Alzheimer's diseas
     13   43   87.8   747 2   JH0773   Alzheimer's diseas

```
14    39    79.6     142    2    E89026              protein F13A2.1 [i
15    35    71.4     774    2    AG1565              autolysin (amidase
16    34    69.4     626    2    AF0358              conserved hypothet
17    34    69.4    3562    2    A47171              chondroitin sulfat
18    34    69.4    4563    1    LPHUB               apolipoprotein B-1
19    33    67.3     927    2    T38127              phosphoprotein - f
20    33    67.3    1245    2    G86404              probable P-glycopr
21    32    65.3     263    2    D84226              hypothetical prote
22    32    65.3     354    2    S51143              FMO-protein - Chlo
23    32    65.3     392    2    T49471              mucin (muc3) relat
24    32    65.3     426    2    G75187              probable trehalose
25    32    65.3     625    2    D86244              protein Ser/Thr pr
26    32    65.3     700    2    E84131              transcription anti
27    32    65.3     929    2    T52517              hypothetical prote
28    32    65.3    1044    2    H97186              glycosyltransferas
29    32    65.3    1265    2    T51498              hypothetical prote
30    32    65.3    1906    2    AD2443              hypothetical prote
31    32    65.3    2514    2    T37320              ataxia telangiecta
32    32    65.3    2619    2    T24588              hypothetical prote
33    31    63.3      87    2    A97842              hypothetical prote
34    31    63.3     155    2    F75040              hypothetical prote
35    31    63.3     178    2    C64168              hypothetical prote
36    31    63.3     182    2    AC0449              conserved hypothet
37    31    63.3     183    2    S56460              probable alpha hel
38    31    63.3     183    2    AD1056              conserved hypothet
39    31    63.3     183    2    C86121              probable alpha hel
40    31    63.3     183    2    C91280              probable alpha hel
41    31    63.3     198    2    S48290              OX40 ligand - mous
42    31    63.3     199    2    F72060              conserved hypothet
43    31    63.3     199    2    C86564              CT471 hypothetical
44    31    63.3     226    2    G69129              hypothetical prote
45    31    63.3     279    2    T41124              single-stranded DN
```

ALIGNMENTS

RESULT 1
E60045
Alzheimer's disease amyloid beta/A4 protein precursor - sheep (fragment)
C;Species: Ovis sp. (sheep)
C;Date: 01-Dec-1992 #sequence_revision 01-Dec-1992 #text_change 28-Jul-1995
C;Accession: E60045
R;Johnstone, E.M.; Chaney, M.O.; Norris, F.H.; Pascual, R.; Little, S.P.
Brain Res. Mol. Brain Res. 10, 299-305, 1991
A;Title: Conservation of the sequence of the Alzheimer's disease amyloid peptide
in dog, polar bear and five other mammals by cross-species polymerase chain
reaction analysis.
A;Reference number: A60045; MUID:92017079; PMID:1656157
A;Accession: E60045
A;Molecule type: mRNA
A;Residues: 1-57 <JOH>
A;Cross-references: EMBL:X56130
C;Superfamily: Alzheimer's disease amyloid beta protein; animal Kunitz-type
proteinase inhibitor homology
C;Keywords: alternative splicing; Alzheimer's disease; amyloid; brain

```
Query Match              100.0%;  Score 49;  DB 2;  Length 57;
Best Local Similarity    100.0%;  Pred. No. 0.0018;
Matches   10;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy        1 SEVKMDAEFR 10
            |||||||||||
Db        1 SEVKMDAEFR 10


RESULT 2
F60045
Alzheimer's disease amyloid beta/A4 protein precursor - pig (fragment)
C;Species: Sus scrofa domestica (domestic pig)
C;Date: 01-Dec-1992 #sequence_revision 01-Dec-1992 #text_change 13-Aug-1999
C;Accession: F60045
R;Johnstone, E.M.; Chaney, M.O.; Norris, F.H.; Pascual, R.; Little, S.P.
Brain Res. Mol. Brain Res. 10, 299-305, 1991
A;Title: Conservation of the sequence of the Alzheimer's disease amyloid peptide
in dog, polar bear and five other mammals by cross-species polymerase chain
reaction analysis.
A;Reference number: A60045; MUID:92017079; PMID:1656157
A;Accession: F60045
A;Molecule type: mRNA
A;Residues: 1-57 <JOH>
A;Cross-references: EMBL:X56127; NID:g1895; PIDN:CAA39592.1; PID:g1896
C;Superfamily: Alzheimer's disease amyloid beta protein; animal Kunitz-type
proteinase inhibitor homology
C;Keywords: alternative splicing; Alzheimer's disease; amyloid; brain

Query Match              100.0%;  Score 49;  DB 2;  Length 57;
Best Local Similarity    100.0%;  Pred. No. 0.0018;
Matches   10;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy        1 SEVKMDAEFR 10
            |||||||||||
Db        1 SEVKMDAEFR 10


RESULT 3
G60045
Alzheimer's disease amyloid beta/A4 protein precursor - guinea pig (fragment)
C;Species: Cavia porcellus (guinea pig)
C;Date: 01-Dec-1992 #sequence_revision 01-Dec-1992 #text_change 28-Jul-1995
C;Accession: G60045
R;Johnstone, E.M.; Chaney, M.O.; Norris, F.H.; Pascual, R.; Little, S.P.
Brain Res. Mol. Brain Res. 10, 299-305, 1991
A;Title: Conservation of the sequence of the Alzheimer's disease amyloid peptide
in dog, polar bear and five other mammals by cross-species polymerase chain
reaction analysis.
A;Reference number: A60045; MUID:92017079; PMID:1656157
A;Accession: G60045
A;Molecule type: mRNA
A;Residues: 1-57 <JOH>
A;Cross-references: EMBL:X56126
C;Superfamily: Alzheimer's disease amyloid beta protein; animal Kunitz-type
proteinase inhibitor homology
C;Keywords: alternative splicing; Alzheimer's disease; amyloid; brain
```

```
Query Match              100.0%;  Score 49;  DB 2;  Length 57;
Best Local Similarity    100.0%;  Pred. No. 0.0018;
Matches   10;  Conservative   0;  Mismatches   0;  Indels   0;  Gaps   0;

Qy       1 SEVKMDAEFR 10
           ||||||||||
Db       1 SEVKMDAEFR 10
```

RESULT 4
D60045
Alzheimer's disease amyloid beta/A4 protein precursor - bovine (fragment)
C;Species: Bos primigenius taurus (cattle)
C;Date: 01-Dec-1992 #sequence_revision 01-Dec-1992 #text_change 28-Jul-1995
C;Accession: D60045
R;Johnstone, E.M.; Chaney, M.O.; Norris, F.H.; Pascual, R.; Little, S.P.
Brain Res. Mol. Brain Res. 10, 299-305, 1991
A;Title: Conservation of the sequence of the Alzheimer's disease amyloid peptide
in dog, polar bear and five other mammals by cross-species polymerase chain
reaction analysis.
A;Reference number: A60045; MUID:92017079; PMID:1656157
A;Accession: D60045
A;Molecule type: mRNA
A;Residues: 1-57 <JOH>
A;Cross-references: EMBL:X56124
C;Superfamily: Alzheimer's disease amyloid beta protein; animal Kunitz-type
proteinase inhibitor homology
C;Keywords: alternative splicing; Alzheimer's disease; amyloid; brain

```
Query Match              100.0%;  Score 49;  DB 2;  Length 57;
Best Local Similarity    100.0%;  Pred. No. 0.0018;
Matches   10;  Conservative   0;  Mismatches   0;  Indels   0;  Gaps   0;

Qy       1 SEVKMDAEFR 10
           ||||||||||
Db       1 SEVKMDAEFR 10
```

RESULT 5
A60045
Alzheimer's disease amyloid beta/A4 protein precursor - dog (fragment)
C;Species: Canis lupus familiaris (dog)
C;Date: 01-Dec-1992 #sequence_revision 01-Dec-1992 #text_change 28-Jul-1995
C;Accession: A60045
R;Johnstone, E.M.; Chaney, M.O.; Norris, F.H.; Pascual, R.; Little, S.P.
Brain Res. Mol. Brain Res. 10, 299-305, 1991
A;Title: Conservation of the sequence of the Alzheimer's disease amyloid peptide
in dog, polar bear and five other mammals by cross-species polymerase chain
reaction analysis.
A;Reference number: A60045; MUID:92017079; PMID:1656157
A;Accession: A60045
A;Molecule type: mRNA
A;Residues: 1-57 <JOH>
A;Cross-references: EMBL:X56125
C;Superfamily: Alzheimer's disease amyloid beta protein; animal Kunitz-type
proteinase inhibitor homology

C;Keywords: alternative splicing; Alzheimer's disease; amyloid; brain

```
   Query Match              100.0%;  Score 49;  DB 2;  Length 57;
   Best Local Similarity    100.0%;  Pred. No. 0.0018;
   Matches    10;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;


Qy         1 SEVKMDAEFR 10
             ||||||||||
Db         1 SEVKMDAEFR 10
```


RESULT 6
B60045
Alzheimer's disease amyloid beta/A4 protein precursor - polar bear (fragment)
C;Species: Ursus maritimus (polar bear)
C;Date: 01-Dec-1992 #sequence_revision 01-Dec-1992 #text_change 13-Aug-1999
C;Accession: B60045
R;Johnstone, E.M.; Chaney, M.O.; Norris, F.H.; Pascual, R.; Little, S.P.
Brain Res. Mol. Brain Res. 10, 299-305, 1991
A;Title: Conservation of the sequence of the Alzheimer's disease amyloid peptide
in dog, polar bear and five other mammals by cross-species polymerase chain
reaction analysis.
A;Reference number: A60045; MUID:92017079; PMID:1656157
A;Accession: B60045
A;Molecule type: mRNA
A;Residues: 1-57 <JOH>
A;Cross-references: EMBL:X56128; NID:g2165; PIDN:CAA39593.1; PID:g2166
C;Superfamily: Alzheimer's disease amyloid beta protein; animal Kunitz-type
proteinase inhibitor homology
C;Keywords: alternative splicing; Alzheimer's disease; amyloid; brain

```
   Query Match              100.0%;  Score 49;  DB 2;  Length 57;
   Best Local Similarity    100.0%;  Pred. No. 0.0018;
   Matches    10;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;


Qy         1 SEVKMDAEFR 10
             ||||||||||
Db         1 SEVKMDAEFR 10
```


RESULT 7
PQ0438
Alzheimer's disease amyloid A4 protein precursor - rabbit (fragment)
C;Species: Oryctolagus cuniculus (domestic rabbit)
C;Date: 30-Sep-1993 #sequence_revision 19-Oct-1995 #text_change 19-Oct-1995
C;Accession: PQ0438; C60045
R;Davidson, J.S.; West, R.L.; Kotikalapudi, P.; Maroun, L.E.
Biochem. Biophys. Res. Commun. 188, 905-911, 1992
A;Title: Sequence and methylation in the beta/A4 region of the rabbit amyloid
precursor protein gene.
A;Reference number: PQ0438; MUID:93075180; PMID:1445331
A;Accession: PQ0438
A;Molecule type: DNA
A;Residues: 1-82 <DAV>
A;Cross-references: GB:M83558; GB:M83657
R;Johnstone, E.M.; Chaney, M.O.; Norris, F.H.; Pascual, R.; Little, S.P.
Brain Res. Mol. Brain Res. 10, 299-305, 1991

A;Title: Conservation of the sequence of the Alzheimer's disease amyloid peptide
in dog, polar bear and five other mammals by cross-species polymerase chain
reaction analysis.
A;Reference number: A60045; MUID:92017079; PMID:1656157
A;Accession: C60045
A;Molecule type: mRNA
A;Residues: 12-68 <JOH>
A;Cross-references: EMBL:X56129
C;Superfamily: Alzheimer's disease amyloid beta protein; animal Kunitz-type
proteinase inhibitor homology
C;Keywords: alternative splicing; Alzheimer's disease; amyloid; Down's syndrome

```
   Query Match              100.0%;  Score 49;  DB 2;  Length 82;
   Best Local Similarity    100.0%;  Pred. No. 0.0027;
   Matches   10;  Conservative   0;  Mismatches   0;  Indels   0;  Gaps   0;

Qy          1 SEVKMDAEFR 10
              ||||||||||
Db         12 SEVKMDAEFR 21
```

RESULT 8
A49795
Alzheimer's disease amyloid beta protein precursor - crab-eating macaque
C;Species: Macaca fascicularis (crab-eating macaque)
C;Date: 10-Sep-1999 #sequence_revision 10-Sep-1999 #text_change 10-Sep-1999
C;Accession: A49795
R;Podlisny, M.B.; Tolan, D.R.; Selkoe, D.J.
Am. J. Pathol. 138, 1423-1435, 1991
A;Title: Homology of the amyloid beta protein precursor in monkey and human
supports a primate model for beta amyloidosis in Alzheimer's disease.
A;Reference number: A49795; MUID:91273117; PMID:1905108
A;Accession: A49795
A;Status: preliminary
A;Molecule type: mRNA
A;Residues: 1-695 <POD>
A;Cross-references: GB:M58727; NID:g342062; PIDN:AAA36829.1; PID:g342063
C;Superfamily: Alzheimer's disease amyloid beta protein; animal Kunitz-type
proteinase inhibitor homology
C;Keywords: alternative splicing

```
   Query Match              100.0%;  Score 49;  DB 1;  Length 695;
   Best Local Similarity    100.0%;  Pred. No. 0.028;
   Matches   10;  Conservative   0;  Mismatches   0;  Indels   0;  Gaps   0;

Qy          1 SEVKMDAEFR 10
              ||||||||||
Db        592 SEVKMDAEFR 601
```

RESULT 9
QRHUA4
Alzheimer's disease amyloid beta protein precursor [validated] - human
N;Alternate names: Alzheimer's disease amyloid A4 protein; coagulation factor
XIa inhibitor; proteinase nexin II (PN-II)

N;Contains: amyloid beta protein long, plaque form; amyloid beta protein short, vascular form; amyloid protein precursor splice form APP(695); amyloid protein precursor splice form APP(751); amyloid protein precursor splice form APP(770)
C;Species: Homo sapiens (man)
C;Date: 30-Jun-1987 #sequence_revision 28-Jul-1995 #text_change 15-Sep-2000
C;Accession: S02260; S05194; A32277; A33260; A35486; I39452; I39451; I39453; I59562; A44017; B44017; A03134; A29030; A47584; A47585; S02638; S00707; S00925; A38949; A30320; B30320; C30320; A31087; A24668; A28583; A29302; A60805; JL0038; S06121; A60355; A59011; A38384; S29076; S38252; S32539; S48148; S48692; S51186; S51185; S51184; S51183; A54238; I58075; I52250; S09010; S10737; S24127; S43644
R;Lemaire, H.G.; Salbaum, J.M.; Multhaup, G.; Kang, J.; Bayney, R.M.; Unterbeck, A.; Beyreuther, K.; Mueller-Hill, B.
Nucleic Acids Res. 17, 517-522, 1989
A;Title: The PreA4(695) precursor protein of Alzheimer's disease A4 amyloid is encoded by 16 exons.
A;Reference number: S02260; MUID:89128427; PMID:2783775
A;Accession: S02260
A;Molecule type: DNA
A;Residues: 1-288,'V',365-770 <LEM1>
A;Cross-references: EMBL:X13466
A;Note: alternative splice form APP(695)
R;Lemaire, H.G.
submitted to the EMBL Data Library, November 1988
A;Reference number: S05194
A;Accession: S05194
A;Molecule type: DNA
A;Residues: 1-14,'VW',17-288,'V',365-770 <LEM2>
A;Cross-references: EMBL:X13466; NID:g35598; PIDN:CAA31830.1; PID:g871360
A;Note: alternative splice form APP(695)
R;La Fauci, G.; Lahiri, D.K.; Salton, S.R.J.; Robakis, N.K.
Biochem. Biophys. Res. Commun. 159, 297-304, 1989
A;Title: Characterization of the 5'-end region and the first two exons of the beta-protein precursor gene.
A;Reference number: A32277; MUID:89165870; PMID:2538123
A;Accession: A32277
A;Molecule type: DNA
A;Residues: 1-75 <LAF>
A;Cross-references: GB:M24546; GB:M24547; NID:g341202; PIDN:AAC13654.1; PID:g516074
R;Johnstone, E.M.; Chaney, M.O.; Moore, R.E.; Ward, K.E.; Norris, F.H.; Little, S.P.
Biochem. Biophys. Res. Commun. 163, 1248-1255, 1989
A;Title: Alzheimer's disease amyloid peptide is encoded by two exons and shows similarity to soybean trypsin inhibitor.
A;Reference number: A33260; MUID:89392030; PMID:2675837
A;Accession: A33260
A;Molecule type: DNA
A;Residues: 656-737 <JOH>
A;Cross-references: GB:M29270; NID:g178863; PIDN:AAA51768.1; PID:g178865
R;Prelli, F.; Levy, E.; van Duinen, S.G.; Bots, G.T.A.M.; Luyendijk, W.; Frangione, B.
Biochem. Biophys. Res. Commun. 170, 301-307, 1990
A;Title: Expression of a normal and variant Alzheimer's beta-protein gene in amyloid of hereditary cerebral hemorrhage, Dutch type: DNA and protein diagnostic assays.
A;Reference number: A35486; MUID:90321244; PMID:2196878
A;Accession: A35486

A;Molecule type: DNA
A;Residues: 672-710 <PRE1>
A;Note: 693-Gln was found in DNA isolated from HCHWA-D patients
R;Yoshikai, S.I.; Sasaki, H.; Doh-ura, K.; Furuya, H.; Sakaki, Y.
Gene 87, 257-263, 1990
A;Title: Genomic organization of the human amyloid beta-protein precursor gene.
A;Reference number: I39451; MUID:90236318; PMID:2110105
A;Accession: I39452
A;Status: nucleic acid sequence not shown; translation not shown; translated
from GB/EMBL/DDBJ
A;Molecule type: DNA
A;Residues: 1-770 <YOS1>
A;Cross-references: GB:M33112; NID:g178613; PIDN:AAB59502.1; PID:g178616
A;Accession: I39451
A;Status: nucleic acid sequence not shown; translation not shown; translated
from GB/EMBL/DDBJ
A;Molecule type: DNA
A;Residues: 1-530,'QWLMPVIPAFWEAKVGR' <YOS2>
A;Cross-references: GB:M34875; NID:g178608; PIDN:AAB59501.1; PID:g178615
R;Yoshikai, S.I.; Sasaki, H.; Doh-ura, K.; Furuya, H.; Sakaki, Y.
Gene 102, 291-292, 1991
A;Reference number: A59020; MUID:91340168; PMID:1908403
A;Contents: annotation; erratum
A;Note: revised physical map for reference I39451
R;Levy, E.; Carman, M.D.; Fernandez-Madrid, I.J.; Power, M.D.; Lieberburg, I.;
van Duinen, S.G.; Bots, G.T.; Luyendijk, W.; Frangione, B.
Science 248, 1124-1126, 1990
A;Title: Mutation of the Alzheimer's disease amyloid gene in hereditary cerebral
hemorrhage, Dutch type.
A;Reference number: I39453; MUID:90260663; PMID:2111584
A;Accession: I39453
A;Status: translated from GB/EMBL/DDBJ
A;Molecule type: DNA
A;Residues: 656-737 <LEV>
A;Cross-references: GB:M37896; NID:g178618; PIDN:AAA51727.1; PID:g178620
A;Note: a mutation with 693-Gln is presented
R;Murrell, J.; Farlow, M.; Ghetti, B.; Benson, M.D.
Science 254, 97-99, 1991
A;Title: A mutation in the amyloid precursor protein associated with hereditary
Alzheimer's disease.
A;Reference number: I59562; MUID:92022553; PMID:1925564
A;Accession: I59562
A;Status: translated from GB/EMBL/DDBJ
A;Molecule type: DNA
A;Residues: 689-716,'F',718-737 <MUR>
A;Cross-references: GB:S57665; NID:g236720; PIDN:AAB19991.1; PID:g236721
R;Kamino, K.; Orr, H.T.; Payami, H.; Wijsman, E.M.; Alonso, M.E.; Pulst, S.M.;
Anderson, L.; O'dahl, S.; Nemens, E.; White, J.A.; Sadovnick, A.D.; Ball, M.J.;
Kaye, J.; Warren, A.; McInnis, M.; Antonarakis, S.E.; Korenberg, J.R.; Sharma,
V.; Kukull, W.; Larson, E.; Heston, L.L.; Martin, G.M.; Bird, T.D.;
Schellenberg, G.D.
Am. J. Hum. Genet. 51, 998-1014, 1992
A;Title: Linkage and mutational analysis of familial Alzheimer disease kindreds
for the APP gene region.
A;Reference number: A44017; MUID:93035397; PMID:1415269
A;Accession: A44017
A;Molecule type: DNA

A;Residues: 687-692,'G',694-718 <KAM1>
A;Cross-references: GB:S45135; NID:g257377; PIDN:AAB23645.1; PID:g257378
A;Experimental source: familial Alzheimer disease family SB
A;Note: sequence extracted from NCBI backbone (NCBIP:115374)
A;Accession: B44017
A;Molecule type: DNA
A;Residues: 687-718 <KAM2>
A;Cross-references: GB:S45136; NID:g257379; PIDN:AAB23646.1; PID:g257380
A;Experimental source: familial Alzheimer disease family LIT
A;Note: sequence extracted from NCBI backbone (NCBIP:115376)
A;Note: this sequence has a silent mutation
R;Kang, J.; Lemaire, H.G.; Unterbeck, A.; Salbaum, J.M.; Masters, C.L.;
Grzeschik, K.H.; Multhaup, G.; Beyreuther, K.; Muller-Hill, B.
Nature 325, 733-736, 1987
A;Title: The precursor of Alzheimer's disease amyloid A4 protein resembles a
cell-surface receptor.
A;Reference number: A03134; MUID:87144572; PMID:2881207
A;Accession: A03134
A;Molecule type: mRNA
A;Residues: 1-288,'V',365-770 <KAN>
A;Cross-references: GB:Y00264; NID:g28525; PIDN:CAA68374.1; PID:g28526
A;Note: alternative splice form APP(695)
R;Robakis, N.K.; Ramakrishna, N.; Wolfe, G.; Wisniewski, H.M.
Proc. Natl. Acad. Sci. U.S.A. 84, 4190-4194, 1987
A;Title: Molecular cloning and characterization of a cDNA encoding the
cerebrovascular and the neuritic plaque amyloid peptides.
A;Reference number: A29030; MUID:87231971; PMID:3035574
A;Accession: A29030
A;Molecule type: mRNA
A;Residues: 284-288,'V',365-646,'E',648-770 <ROB>
A;Cross-references: GB:M16765; NID:g178539; PIDN:AAA51722.1; PID:g178540
A;Note: the authors translated the codon GAG for residue 647 as Asp
R;Goldgaber, D.; Lerman, M.I.; McBride, O.W.; Saffiotti, U.; Gajdusek, D.C.
Science 235, 877-880, 1987
A;Title: Characterization and chromosomal localization of a cDNA encoding brain
amyloid of Alzheimer's disease.
A;Reference number: A47584; MUID:87120328; PMID:3810169
A;Accession: A47584
A;Molecule type: mRNA
A;Residues: 674-756,'S',758-770 <GOL>
A;Cross-references: GB:M15533; NID:g178706; PIDN:AAA35540.1; PID:g178707
A;Experimental source: brain
R;Tanzi, R.E.; Gusella, J.F.; Watkins, P.C.; Bruns, G.A.P.; St George-Hyslop,
P.; Van Keuren, M.L.; Patterson, D.; Pagan, S.; Kurnit, D.M.; Neve, R.L.
Science 235, 880-884, 1987
A;Title: Amyloid beta protein gene: cDNA, mRNA distribution, and genetic linkage
near the Alzheimer locus.
A;Reference number: A47585; MUID:87120329; PMID:2949367
A;Accession: A47585
A;Molecule type: mRNA
A;Residues: 674-703 <TAN1>
A;Cross-references: GB:M15532; NID:g177957; PIDN:AAA51564.1; PID:g177958
R;Dyrks, T.; Weidemann, A.; Multhaup, G.; Salbaum, J.M.; Lemaire, H.G.; Kang,
J.; Mueller-Hill, B.; Masters, C.L.; Beyreuther, K.
EMBO J. 7, 949-957, 1988
A;Title: Identification, transmembrane orientation and biogenesis of the amyloid
A4 precursor of Alzheimer's disease.

A;Reference number: S02638; MUID:88296437; PMID:2900137
A;Accession: S02638
A;Molecule type: mRNA
A;Residues: 672-678 <DYR>
R;Tanzi, R.E.; McClatchey, A.I.; Lamperti, E.D.; Villa-Komaroff, L.; Gusella,
J.F.; Neve, R.L.
Nature 331, 528-530, 1988
A;Title: Protease inhibitor domain encoded by an amyloid protein precursor mRNA
associated with Alzheimer's disease.
A;Reference number: S00707; MUID:88122640; PMID:2893290
A;Accession: S00707
A;Molecule type: mRNA
A;Residues: 286-344,'I',365-366 <TAN2>
A;Cross-references: EMBL:X06982; NID:g28817; PIDN:CAA30042.1; PID:g929612
A;Experimental source: promyelocytic leukemia cell line HL60
A;Note: alternative splice form APP(751)
R;Ponte, P.; Gonzalez-DeWhitt, P.; Schilling, J.; Miller, J.; Hsu, D.;
Greenberg, B.; Davis, K.; Wallace, W.; Lieberburg, I.; Fuller, F.; Cordell, B.
Nature 331, 525-527, 1988
A;Title: A new A4 amyloid mRNA contains a domain homologous to serine proteinase
inhibitors.
A;Reference number: S00925; MUID:88122639; PMID:2893289
A;Accession: S00925
A;Molecule type: mRNA
A;Residues: 1-344,'I',365-770 <PO2>
A;Cross-references: GB:X06989; EMBL:Y00297; NID:g28720; PIDN:CAA30050.1;
PID:g28721
A;Note: alternative splice form APP(751)
R;Kitaguchi, N.; Takahashi, Y.; Tokushima, Y.; Shiojiri, S.; Ito, H.
Nature 331, 530-532, 1988
A;Title: Novel precursor of Alzheimer's disease amyloid protein shows protease
inhibitory activity.
A;Reference number: A38949; MUID:88122641; PMID:2893291
A;Accession: A38949
A;Molecule type: mRNA
A;Residues: 287-367 <KIT>
A;Cross-references: GB:X06981; NID:g28816; PIDN:CAA30041.1; PID:g929611
A;Experimental source: glioblastoma cell line
A;Note: alternative splice form APP(770)
R;Vitek, M.P.; Rasool, C.G.; de Sauvage, F.; Vitek, S.M.; Bartus, R.T.; Beer,
B.; Ashton, R.A.; Macq, A.F.; Maloteaux, J.M.; Blume, A.J.; Octave, J.N.
Brain Res. Mol. Brain Res. 4, 121-131, 1988
A;Title: Absence of mutation in the beta-amyloid cDNAs cloned from the brains of
three patients with sporadic Alzheimer's disease.
A;Reference number: A30320
A;Accession: A30320
A;Status: not compared with conceptual translation
A;Molecule type: mRNA
A;Residues: 284-288,'V',365-770 <VIT1>
A;Accession: B30320
A;Status: not compared with conceptual translation
A;Molecule type: mRNA
A;Residues: 122-288,'V',365-770 <VIT2>
A;Accession: C30320
A;Status: not compared with conceptual translation
A;Molecule type: mRNA
A;Residues: 606-770 <VIT3>

R;Zain, S.B.; Salim, M.; Chou, W.G.; Sajdel-Sulkowska, E.M.; Majocha, R.E.;
Marotta, C.A.
Proc. Natl. Acad. Sci. U.S.A. 85, 929-933, 1988
A;Title: Molecular cloning of amyloid cDNA derived from mRNA of the Alzheimer
disease brain: coding and noncoding regions of the fetal precursor mRNA are
expressed in the cortex.
A;Reference number: A31087; MUID:88124954; PMID:2893379
A;Accession: A31087
A;Molecule type: mRNA
A;Residues: 507-770 <ZAI>
A;Cross-references: GB:M18734; NID:g178572; PIDN:AAA51726.1; PID:g178573
A;Note: the authors translated the codon GAA for residue 599 as Gly, ACC for
residue 603 as Val, GTG for residue 604 as Glu, GAG for residue 605 as Leu, CTT
for residue 607 as Pro, CCC for residue 608 as Val, GTG for residue 609 as Asn,
AAT for residue 610 as Gly, and GGT for residue 655 as Ser
A;Note: the cited Genbank accession number, J03594, is not in release 101.0
R;Masters, C.L.; Multhaup, G.; Simms, G.; Pottgiesser, J.; Martins, R.N.;
Beyreuther, K.

```
   Query Match              100.0%;  Score 49;  DB 1;  Length 770;
   Best Local Similarity    100.0%;  Pred. No. 0.032;
   Matches   10;  Conservative   0;  Mismatches   0;  Indels   0;  Gaps   0;

Qy         1 SEVKMDAEFR 10
             ||||||||||
Db       667 SEVKMDAEFR 676
```

RESULT 10
S23094
beta-amyloid protein precursor - rat
C;Species: Rattus norvegicus (Norway rat)
C;Date: 22-Nov-1993 #sequence_revision 10-Nov-1995 #text_change 03-May-1996
C;Accession: S23094
R;Kojima, S.; Omori, M.
FEBS Lett. 304, 57-60, 1992
A;Title: Two-way cleavage of beta-amyloid protein precursor by multicatalytic
proteinase.
A;Reference number: S23094; MUID:92316198; PMID:1618299
A;Accession: S23094
A;Molecule type: protein
A;Residues: 1-33 <KOJ>
C;Superfamily: Alzheimer's disease amyloid beta protein; animal Kunitz-type
proteinase inhibitor homology

```
   Query Match              89.8%;  Score 44;  DB 2;  Length 33;
   Best Local Similarity    100.0%;  Pred. No. 0.011;
   Matches    9;  Conservative   0;  Mismatches   0;  Indels   0;  Gaps   0;

Qy         1 SEVKMDAEF 9
             |||||||||
Db         1 SEVKMDAEF 9
```

RESULT 11
A27485
Alzheimer's disease amyloid beta/A4 protein homolog precursor - mouse

N;Alternate names: proteinase nexin II
C;Species: Mus musculus (house mouse)
C;Date: 31-Mar-1989 #sequence_revision 31-Mar-1989 #text_change 13-Aug-1999
C;Accession: A27485; S19727; I49485
R;Yamada, T.; Sasaki, H.; Furuya, H.; Miyata, T.; Goto, I.; Sakaki, Y.
Biochem. Biophys. Res. Commun. 149, 665-671, 1987
A;Title: Complementary DNA for the mouse homolog of the human amyloid beta
protein precursor.
A;Reference number: A27485; MUID:88106489; PMID:3322280
A;Accession: A27485
A;Molecule type: mRNA
A;Residues: 1-695 <YAM>
A;Cross-references: GB:M18373; NID:g191568; PIDN:AAA37139.1; PID:g309085
A;Experimental source: brain
R;de Strooper, B.; van Leuven, F.; van den Berghe, H.
Biochim. Biophys. Acta 1129, 141-143, 1991
A;Title: The amyloid beta protein precursor or proteinase nexin II from mouse is
closer related to its human homolog than previously reported.
A;Reference number: S19727; MUID:92096458; PMID:1756177
A;Accession: S19727
A;Molecule type: mRNA
A;Residues: 1-210,'G',212-220,'S',222-396,'A',398-402,'T',404-448,'A',450-695
<STR>
A;Cross-references: EMBL:X59379
R;Izumi, R.; Yamada, T.; Yoshikai, S.; Sasaki, H.; Hattori, M.; Sakaki, Y.
Gene 112, 189-195, 1992
A;Title: Positive and negative regulatory elements for the expression of the
Alzheimer's disease amyloid precursor-encoding gene in mouse.
A;Reference number: I49485; MUID:92209998; PMID:1555768
A;Accession: I49485
A;Status: translated from GB/EMBL/DDBJ
A;Molecule type: DNA
A;Residues: 1-19 <RES>
A;Cross-references: GB:D10603; NID:g220328; PIDN:BAA01456.1; PID:g220329
C;Genetics:
A;Map position: 16C3
C;Superfamily: Alzheimer's disease amyloid beta protein; animal Kunitz-type
proteinase inhibitor homology
C;Keywords: alternative splicing; amyloid; transmembrane protein

```
  Query Match              89.8%;  Score 44;  DB 2;  Length 695;
  Best Local Similarity   100.0%;  Pred. No. 0.33;
  Matches     9;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;


Qy        1 SEVKMDAEF 9
            |||||||||
Db      592 SEVKMDAEF 600
```


RESULT 12
S00550
Alzheimer's disease amyloid beta protein precursor - rat
N;Alternate names: beta-A4 amyloid protein
C;Species: Rattus norvegicus (Norway rat)
C;Date: 30-Jun-1989 #sequence_revision 30-Jun-1989 #text_change 13-Aug-1999
C;Accession: S00550; A41245; A39820; S46251

R;Shivers, B.D.; Hilbich, C.; Multhaup, G.; Salbaum, M.; Beyreuther, K.;
Seeburg, P.H.
EMBO J. 7, 1365-1370, 1988
A;Title: Alzheimer's disease amyloidogenic glycoprotein: expression pattern in
rat brain suggests a role in cell contact.
A;Reference number: S00550; MUID:88312583; PMID:2900758
A;Accession: S00550
A;Molecule type: mRNA
A;Residues: 1-695 <SHI>
A;Cross-references: EMBL:X07648; NID:g55616; PIDN:CAA30488.1; PID:g55617
R;Schubert, D.; Schroeder, R.; LaCorbiere, M.; Saitoh, T.; Cole, G.
Science 241, 223-226, 1988
A;Title: Amyloid beta protein precursor is possibly a heparan sulfate
proteoglycan core protein.
A;Reference number: A41245; MUID:88264430; PMID:2968652
A;Accession: A41245
A;Molecule type: protein
A;Residues: 18-37,'X',39-40,'X',42-44 <SCH>
A;Note: evidence for heparan sulfate attachment
R;Hesse, L.; Beher, D.; Masters, C.L.; Multhaup, G.
FEBS Lett. 349, 109-116, 1994
A;Title: The beta-A4 amyloid precursor protein binding to copper.
A;Reference number: S46251; MUID:94320627; PMID:7913895
A;Contents: annotation; copper binding sites
A;Note: rat peptides were isolated but not sequenced
R;Potempska, A.; Styles, J.; Mehta, P.; Kim, K.S.; Miller, D.L.
J. Biol. Chem. 266, 8464-8469, 1991
A;Title: Purification and tissue level of the beta-amyloid peptide precursor of
rat brain.
A;Reference number: A39820; MUID:91217087; PMID:1673681
A;Accession: A39820
A;Status: preliminary
A;Molecule type: protein
A;Residues: 18-32 <POT>
A;Experimental source: brain
C;Comment: Deposition of amyloid protein as neurofibrillary tangles and/or
plaques is characteristic of both Alzheimer's disease and Down's syndrome.
C;Superfamily: Alzheimer's disease amyloid beta protein; animal Kunitz-type
proteinase inhibitor homology
C;Keywords: alternative splicing; amyloid; glycoprotein; transmembrane protein
F;625-648/Domain: transmembrane #status predicted <TMM>

```
   Query Match              89.8%;  Score 44;  DB 2;  Length 695;
   Best Local Similarity   100.0%;  Pred. No. 0.33;
   Matches    9;  Conservative   0;  Mismatches   0;  Indels   0;  Gaps   0;

Qy         1 SEVKMDAEF 9
             |||||||||
Db       592 SEVKMDAEF 600
```

RESULT 13
JH0773
Alzheimer's disease amyloid beta protein precursor - African clawed frog
C;Species: Xenopus laevis (African clawed frog)
C;Date: 10-Jun-1993 #sequence_revision 10-Jun-1993 #text_change 13-Aug-1999
C;Accession: JH0773

R;Okado, H.; Okamoto, H.
Biochem. Biophys. Res. Commun. 189, 1561-1568, 1992
A;Title: A Xenopus homologue of the human beta-amyloid precursor protein:
developmental regulation of its gene expression.
A;Reference number: JH0773; MUID:93129227; PMID:1282805
A;Accession: JH0773
A;Molecule type: mRNA
A;Residues: 1-747 <OKA>
A;Cross-references: GB:S52417; NID:g263150; PIDN:AAB24853.1; PID:g263151
A;Experimental source: larva
C;Superfamily: Alzheimer's disease amyloid beta protein; animal Kunitz-type
proteinase inhibitor homology
C;Keywords: alternative splicing; amyloid
F;287-337/Domain: animal Kunitz-type proteinase inhibitor homology <BPI>

```
    Query Match              87.8%;  Score 43;  DB 2;  Length 747;
    Best Local Similarity    80.0%;  Pred. No. 0.59;
    Matches    8;  Conservative    2;  Mismatches    0;  Indels    0;  Gaps    0;


Qy          1 SEVKMDAEFR 10
              ||||||:|:|
Db        644 SEVKMDSEYR 653
```

RESULT 14
E89026
protein F13A2.1 [imported] - Caenorhabditis elegans
C;Species: Caenorhabditis elegans
C;Date: 10-May-2001 #sequence_revision 10-May-2001 #text_change 10-May-2001
C;Accession: E89026
R;anonymous, The C. elegans Sequencing Consortium.
Science 282, 2012-2018, 1998
A;Title: Genome sequence of the nematode C. elegans: a platform for
investigating biology.
A;Reference number: A75000; MUID:99069613; PMID:9851916
A;Note: see websites genome.wustl.edu/gsc/C_elegans/ and
www_sanger.ac.uk/Projects/C_elegans/ for a list of authors
A;Note: published errata appeared in Science 283, 35, 1999; Science 283, 2103,
1999; and Science 285, 1493, 1999
A;Accession: E89026
A;Status: preliminary
A;Molecule type: DNA
A;Residues: 1-142 <STO>
A;Cross-references: GB:chr_V; PIDN:AAB69895.1; PID:g2384795; GSPDB:GN00023;
CESP:F13A2.1
C;Genetics:
A;Gene: F13A2.1
A;Map position: 5

```
    Query Match              79.6%;  Score 39;  DB 2;  Length 142;
    Best Local Similarity    77.8%;  Pred. No. 0.67;
    Matches    7;  Conservative    1;  Mismatches    1;  Indels    0;  Gaps    0;


Qy          2 EVKMDAEFR 10
              |:| |||||
Db         56 EIKQDAEFR 64
```

RESULT 15
AG1565
autolysin (amidase) homolog lin1064 [imported] - Listeria innocua (strain
Clip11262)
C;Species: Listeria innocua
C;Date: 27-Nov-2001 #sequence_revision 27-Nov-2001 #text_change 27-Nov-2001
C;Accession: AG1565
R;Glaser, P.; Frangeul, L.; Buchrieser, C.; Amend, A.; Baquero, F.; Berche, P.;
Bloecker, H.; Brandt, P.; Chakraborty, T.; Charbit, A.; Chetouani, F.; Couve,
E.; de Daruvar, A.; Dehoux, P.; Domann, E.; Dominguez-Bernal, G.; Duchaud, E.;
Durand, L.; Dussurget, O.; Entian, K.D.; Fsihi, H.; Garcia-Del Portillo, F.;
Garrido, P.; Gautier, L.; Goebel, W.; Gomez-Lopez, N.; Hain, T.; Hauf, J.;
Jackson, D.; Jones, L.M.; Karst, U.
Science 294, 849-852, 2001
A;Authors: Kreft, J.; Kuhn, M.; Kunst, F.; Kurapkat, G.; Madueno, E.;
Maitournam, A.; Mata Vicente, J.; Ng, E.; Nordsiek, G.; Novella, S.; de Pablos,
B.; Perez-Diaz, J.C.; Remmel, B.; Rose, M.; Rusniok, C.; Schlueter, T.; Simoes,
N.; Tierrez, A.; Vazquez-Boland, J.A.; Voss, H.; Wehland, J.; Cossart, P.
A;Title: Comparative genomics of Listeria species.
A;Reference number: AB1077; MUID:21537279; PMID:11679669
A;Accession: AG1565
A;Status: preliminary
A;Molecule type: DNA
A;Residues: 1-774 <GLA>
A;Cross-references: GB:AL592022; PIDN:CAC96295.1; PID:g16413523; GSPDB:GN00178
A;Experimental source: strain Clip11262
C;Genetics:
A;Gene: lin1064

    Query Match   71.4%; Score 35; DB 2; Length 774;
    Best Local Similarity   75.0%; Pred. No. 32;
    Matches   6; Conservative   2; Mismatches   0; Indels   0; Gaps   0;

Qy   3 VKMDAEFR 10
              :|:|||||
Db   123 IKIDAEFR 130

Search completed: January 21, 2004, 09:26:08
Job time : 1.91778 secs

GenCore version 5.1.6
Copyright (c) 1993 - 2004 Compugen Ltd.

OM protein - protein search, using sw model

Run on: January 21, 2004, 09:25:15 ; Search time 2.00765 Seconds
                                             (without alignments)
                                             1018.511 Million cell updates/sec

Title: US-09-869-414A-64
Perfect score: 49
Sequence: 1 SEVKMDAEFR 10

Scoring table: BLOSUM62
                Gapop 10.0 , Gapext 0.5

Searched: 762491 seqs, 204481190 residues

Total number of hits satisfying chosen parameters: 762491

Minimum DB seq length: 0
Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%
                 Maximum Match 100%
                 Listing first 45 summaries

Database :   Published_Applications_AA:*
           1:   /cgn2_6/ptodata/2/pubpaa/US07_PUBCOMB.pep:*
           2:   /cgn2_6/ptodata/2/pubpaa/PCT_NEW_PUB.pep:*
           3:   /cgn2_6/ptodata/2/pubpaa/US06_NEW_PUB.pep:*
           4:   /cgn2_6/ptodata/2/pubpaa/US06_PUBCOMB.pep:*
           5:   /cgn2_6/ptodata/2/pubpaa/US07_NEW_PUB.pep:*
           6:   /cgn2_6/ptodata/2/pubpaa/PCTUS_PUBCOMB.pep:*
           7:   /cgn2_6/ptodata/2/pubpaa/US08_NEW_PUB.pep:*
           8:   /cgn2_6/ptodata/2/pubpaa/US08_PUBCOMB.pep:*
           9:   /cgn2_6/ptodata/2/pubpaa/US09A_PUBCOMB.pep:*
          10:   /cgn2_6/ptodata/2/pubpaa/US09B_PUBCOMB.pep:*
          11:   /cgn2_6/ptodata/2/pubpaa/US09C_PUBCOMB.pep:*
          12:   /cgn2_6/ptodata/2/pubpaa/US09_NEW_PUB.pep:*
          13:   /cgn2_6/ptodata/2/pubpaa/US10A_PUBCOMB.pep:*
          14:   /cgn2_6/ptodata/2/pubpaa/US10B_PUBCOMB.pep:*
          15:   /cgn2_6/ptodata/2/pubpaa/US10C_PUBCOMB.pep:*
          16:   /cgn2_6/ptodata/2/pubpaa/US10_NEW_PUB.pep:*
          17:   /cgn2_6/ptodata/2/pubpaa/US60_NEW_PUB.pep:*
          18:   /cgn2_6/ptodata/2/pubpaa/US60_PUBCOMB.pep:*

        Pred. No. is the number of results predicted by chance to have a
        score greater than or equal to the score of the result being printed,
        and is derived by analysis of the total score distribution.

                              SUMMARIES
                         %
Result   Query
  No.   Score   Match Length DB   ID   Description

```
-------------------------------------------------------------------------------
     1      49    100.0      10    9    US-09-794-927-64          Sequence 64, Appl
     2      49    100.0      10    9    US-09-795-847-64         'Sequence 64, Appl
     3      49    100.0      10    9    US-09-794-743-64          Sequence 64, Appl
     4      49    100.0      10    9    US-09-794-748-64          Sequence 64, Appl
     5      49    100.0      10    9    US-09-796-264-4           Sequence 4, Appli
     6      49    100.0      10    9    US-09-794-925-64          Sequence 64, Appl
     7      49    100.0      10    9    US-09-681-442-64          Sequence 64, Appl
     8      49    100.0      10   10    US-09-845-226-4            Sequence 4, Appli
     9      49    100.0      10   10    US-09-795-903A-4          Sequence 4, Appli
    10      49    100.0      10   11    US-09-869-414-64          Sequence 64, Appl
    11      49    100.0      10   11    US-09-548-366-64          Sequence 64, Appl
    12      49    100.0      10   12    US-10-427-208-53          Sequence 53, Appl
    13      49    100.0      10   15    US-10-032-818-7           Sequence 7, Appli
    14      49    100.0      11   12    US-10-354-955-1           Sequence 1, Appli
    15      49    100.0      11   12    US-10-354-955-3           Sequence 3, Appli
    16      49    100.0      12    9    US-09-896-874-2         Sequence 2, Appli
    17      49    100.0      12   10    US-09-896-139-2           Sequence 2, Appli
    18      49    100.0      12   10    US-09-895-843-2           Sequence 2, Appli
    19      49    100.0      12   11    US-09-895-871-2           Sequence 2, Appli
    20      49    100.0      12   12    US-10-427-208-54          Sequence 54, Appl
    21      49    100.0      13   12    US-10-160-777-2           Sequence 2, Appli
    22      49    100.0      13   12    US-10-337-075-2           Sequence 2, Appli
    23      49    100.0      13   15    US-10-084-380A-7          Sequence 7, Appli
    24      49    100.0      13   15    US-10-192-625-2           Sequence 2, Appli
    25      49    100.0      13   15    US-10-192-424-2           Sequence 2, Appli
    26      49    100.0      13   15    US-10-183-126A-2          Sequence 2, Appli
    27      49    100.0      13   15    US-10-171-343-2           Sequence 2, Appli
    28      49    100.0      13   15    US-10-264-707-2           Sequence 2, Appli
    29      49    100.0      14   12    US-10-427-208-55          Sequence 55, Appl
    30      49    100.0      16   12    US-10-427-208-56          Sequence 56, Appl
    31      49    100.0      23   12    US-10-354-955-6           Sequence 6, Appli
    32      49    100.0      67   12    US-10-437-706-1           Sequence 1, Appli
    33      49    100.0      82   11    US-09-848-616-173         Sequence 173, App
    34      49    100.0      82   12    US-10-050-898-219         Sequence 219, App
    35      49    100.0      82   12    US-10-050-902-219         Sequence 219, App
    36      49    100.0     534   12    US-09-998-491-2           Sequence 2, Appli
    37      49    100.0     695    9    US-09-794-927-10          Sequence 10, Appl
    38      49    100.0     695    9    US-09-794-927-14          Sequence 14, Appl
    39      49    100.0     695    9    US-09-795-847-10          Sequence 10, Appl
    40      49    100.0     695    9    US-09-795-847-14          Sequence 14, Appl
    41      49    100.0     695    9    US-09-794-743-10          Sequence 10, Appl
    42      49    100.0     695    9    US-09-794-743-14          Sequence 14, Appl
    43      49    100.0     695    9    US-09-794-748-10          Sequence 10, Appl
    44      49    100.0     695    9    US-09-794-748-14          Sequence 14, Appl
    45      49    100.0     695    9    US-09-794-925-10          Sequence 10, Appl
```

                              ALIGNMENTS

RESULT 1
US-09-794-927-64
; Sequence 64, Application US/09794927
; Patent No. US20010016324A1
; GENERAL INFORMATION:
; APPLICANT: Gurney, Mark E.

;   APPLICANT: Bienkowski, Michael J.
;   APPLICANT: Heinrikson, Robert L.
;   APPLICANT: Parodi, Luis A.
;   APPLICANT: Yan, Riqiang
;   TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR,
AND
;   TITLE OF INVENTION: USES
;   TITLE OF INVENTION: THEREFOR
;   FILE REFERENCE: 28341/6280FG
;   CURRENT APPLICATION NUMBER: US/09/794,927
;   CURRENT FILING DATE: 2001-02-27
;   PRIOR APPLICATION NUMBER: 09/416,901
;   PRIOR FILING DATE: 1999-10-13
;   PRIOR APPLICATION NUMBER: 60/155,493
;   PRIOR FILING DATE: 1999-09-23
;   PRIOR APPLICATION NUMBER: 09/404,133
;   PRIOR FILING DATE: 1999-09-23
;   PRIOR APPLICATION NUMBER: PCT/US99/20881
;   PRIOR FILING DATE: 1999-09-23
;   PRIOR APPLICATION NUMBER: 60/101,594
;   PRIOR FILING DATE: 1998-09-24
;   NUMBER OF SEQ ID NOS: 73
;   SOFTWARE: PatentIn Ver. 2.0
; SEQ ID NO 64
;   LENGTH: 10
;   TYPE: PRT
;   ORGANISM: Artificial Sequence
;   FEATURE:
;   OTHER INFORMATION: Description of Artificial Sequence: synthetic
US-09-794-927-64

   Query Match   100.0%;   Score 49;   DB 9;   Length 10;
   Best Local Similarity 100.0%;   Pred. No. 0.0017;
   Matches   10; Conservative   0; Mismatches   0; Indels   0; Gaps   0;

Qy   1 SEVKMDAEFR 10
              | | | | | | | | | |
Db   1 SEVKMDAEFR 10

RESULT 2
US-09-795-847-64
; Sequence 64, Application US/09795847
; Patent No. US20010018208A1
; GENERAL INFORMATION:
;   APPLICANT: Gurney, Mark E.
;   APPLICANT: Bienkowski, Michael J.
;   APPLICANT: Heinrikson, Robert L.
;   APPLICANT: Parodi, Luis A.
;   APPLICANT: Yan, Riqiang
;   TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR,
AND
;   TITLE OF INVENTION: USES
;   TITLE OF INVENTION: THEREFOR
;   FILE REFERENCE: 28341/6280DE
;   CURRENT APPLICATION NUMBER: US/09/795,847
;   CURRENT FILING DATE: 2001-02-28

```
;    PRIOR APPLICATION NUMBER:  09/416,901
;    PRIOR FILING DATE:  1999-10-13
;    PRIOR APPLICATION NUMBER:  60/155,493
;    PRIOR FILING DATE:  1999-09-23
;    PRIOR APPLICATION NUMBER:  09/404,133
;    PRIOR FILING DATE:  1999-09-23
;    PRIOR APPLICATION NUMBER:  PCT/US99/20881
;    PRIOR FILING DATE:  1999-09-23
;    PRIOR APPLICATION NUMBER:  60/101,594
;    PRIOR FILING DATE:  1998-09-24
;    NUMBER OF SEQ ID NOS:  73
;    SOFTWARE:  PatentIn Ver. 2.0
;  SEQ ID NO 64
;    LENGTH: 10
;    TYPE: PRT
;    ORGANISM: Artificial Sequence
;    FEATURE:
;    OTHER INFORMATION: Description of Artificial Sequence: synthetic
US-09-795-847-64

   Query Match              100.0%;   Score 49;   DB 9;   Length 10;
   Best Local Similarity    100.0%;   Pred. No. 0.0017;
   Matches   10;  Conservative   0;  Mismatches   0;  Indels   0;  Gaps   0;


Qy          1 SEVKMDAEFR 10
              ||||||||||
Db          1 SEVKMDAEFR 10



RESULT 3
US-09-794-743-64
; Sequence 64, Application US/09794743
; Patent No. US20010021391A1
; GENERAL INFORMATION:
;  APPLICANT:  Gurney, Mark E.
;  APPLICANT:  Bienkowski, Michael J.
;  APPLICANT:  Heinrikson, Robert L.
;  APPLICANT:  Parodi, Luis A.
;  APPLICANT:  Yan, Riqiang
;  TITLE OF INVENTION:  ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR,
AND
;  TITLE OF INVENTION:  USES
;  TITLE OF INVENTION:  THEREFOR
;  FILE REFERENCE:  28341/6280BC
;  CURRENT APPLICATION NUMBER: US/09/794,743
;  CURRENT FILING DATE:  2001-02-27
;  PRIOR APPLICATION NUMBER:  09/416,901
;  PRIOR FILING DATE:  1999-10-13
;  PRIOR APPLICATION NUMBER:  60/155,493
;  PRIOR FILING DATE:  1999-09-23
;  PRIOR APPLICATION NUMBER:  09/404,133
;  PRIOR FILING DATE:  1999-09-23
;  PRIOR APPLICATION NUMBER:  PCT/US99/20881
;  PRIOR FILING DATE:  1999-09-23
;  PRIOR APPLICATION NUMBER:  60/101,594
;  PRIOR FILING DATE:  1998-09-24
;  NUMBER OF SEQ ID NOS:  73
```

; SOFTWARE: PatentIn Ver. 2.0
; SEQ ID NO 64
; LENGTH: 10
; TYPE: PRT
; ORGANISM: Artificial Sequence
; FEATURE:
; OTHER INFORMATION: Description of Artificial Sequence: synthetic
US-09-794-743-64

    Query Match   100.0%; Score 49; DB 9; Length 10;
    Best Local Similarity 100.0%; Pred. No. 0.0017;
    Matches 10; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy   1 SEVKMDAEFR 10
            | | | | | | | | | |
Db   1 SEVKMDAEFR 10

RESULT 4
US-09-794-748-64
; Sequence 64, Application US/09794748
; Patent No. US20020037315A1
; GENERAL INFORMATION:
; APPLICANT: Gurney, Mark E.
; APPLICANT: Bienkowski, Michael J.
; APPLICANT: Heinrikson, Robert L.
; APPLICANT: Parodi, Luis A.
; APPLICANT: Yan, Riqiang
; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR,
AND
; TITLE OF INVENTION: USES
; TITLE OF INVENTION: THEREFOR
; FILE REFERENCE: 28341/6280JL
; CURRENT APPLICATION NUMBER: US/09/794,748
; CURRENT FILING DATE: 2001-02-27
; PRIOR APPLICATION NUMBER: 09/416,901
; PRIOR FILING DATE: 1999-10-13
; PRIOR APPLICATION NUMBER: 60/155,493
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: 09/404,133
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: PCT/US99/20881
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: 60/101,594
; PRIOR FILING DATE: 1998-09-24
; NUMBER OF SEQ ID NOS: 73
; SOFTWARE: PatentIn Ver. 2.0
; SEQ ID NO 64
; LENGTH: 10
; TYPE: PRT
; ORGANISM: Artificial Sequence
; FEATURE:
; OTHER INFORMATION: Description of Artificial Sequence: synthetic
US-09-794-748-64

    Query Match   100.0%; Score 49; DB 9; Length 10;
    Best Local Similarity 100.0%; Pred. No. 0.0017;

```
      Matches   10;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy        1 SEVKMDAEFR 10
            ||||||||||
Db        1 SEVKMDAEFR 10


RESULT 5
US-09-796-264-4
; Sequence 4, Application US/09796264
; Patent No. US20020049303A1
; GENERAL INFORMATION:
;  APPLICANT: Tang, Jordan J.N.
;  APPLICANT:  Lin, Xinli
;  APPLICANT:  Koelsch, Gerald
;  TITLE OF INVENTION: Catalytically Active Recombinant Memapsin and Methods
;  TITLE OF INVENTION:  of Use Thereof
;  FILE REFERENCE: OMRF 179
;  CURRENT APPLICATION NUMBER: US/09/796,264
;  CURRENT FILING DATE:  2001-02-28
;  PRIOR APPLICATION NUMBER: 09/604,608
;  PRIOR FILING DATE: 2000-06-27
;  PRIOR APPLICATION NUMBER: 60/168,060
;  PRIOR FILING DATE: 1999-11-30
;  PRIOR APPLICATION NUMBER: 60/177,836
;  PRIOR FILING DATE: 2000-01-25
;  PRIOR APPLICATION NUMBER: 60/178,368
;  PRIOR FILING DATE: 2000-01-27
;  PRIOR APPLICATION NUMBER: 60/210,292
;  PRIOR FILING DATE: 2000-06-08
;  NUMBER OF SEQ ID NOS: 31
;  SOFTWARE: PatentIn Ver. 2.1
; SEQ ID NO 4
;  LENGTH: 10
;  TYPE: PRT
;  ORGANISM: Artificial Sequence
;  FEATURE:
;  OTHER INFORMATION: Description of Artificial Sequence: Primer
US-09-796-264-4

  Query Match              100.0%;  Score 49;  DB 9;  Length 10;
  Best Local Similarity    100.0%;  Pred. No. 0.0017;
  Matches   10;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy        1 SEVKMDAEFR 10
            ||||||||||
Db        1 SEVKMDAEFR 10


RESULT 6
US-09-794-925-64
; Sequence 64, Application US/09794925
; Patent No. US20020064819A1
; GENERAL INFORMATION:
;  APPLICANT:  Gurney, Mark E.
;  APPLICANT:  Bienkowski, Michael J.
;  APPLICANT:  Heinrikson, Robert L.
```

```
   Query Match              100.0%;  Score 49;  DB 9;  Length 10;
   Best Local Similarity    100.0%;  Pred. No. 0.0017;
   Matches    10;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;


Qy         1 SEVKMDAEFR 10
             ||||||||||
Db         1 SEVKMDAEFR 10
```

; PRIOR APPLICATION NUMBER: 09/404,133
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: PCT/US99/20881
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: 60/101,594
; PRIOR FILING DATE: 1998-09-24   .
; NUMBER OF SEQ ID NOS: 73
; SOFTWARE: PatentIn Ver. 2.0
; SEQ ID NO 64
;   LENGTH: 10
;   TYPE: PRT
;   ORGANISM: Artificial Sequence
;   FEATURE:
;   OTHER INFORMATION: Description of Artificial Sequence: synthetic
US-09-681-442-64

  Query Match   100.0%; Score 49; DB 9; Length 10;
  Best Local Similarity   100.0%; Pred. No. 0.0017;
  Matches   10; Conservative   0; Mismatches   0; Indels   0; Gaps   0;   ·

Qy   1 SEVKMDAEFR 10
             ||||||||||
Db   1 SEVKMDAEFR 10

RESULT 8
US-09-845-226-4
; Sequence 4, Application US/09845226
; Patent No. US20020115600A1
; GENERAL INFORMATION:
; APPLICANT: Tang, Jordan J.N.
; APPLICANT: Hong, Lin
; APPLICANT: Ghosh, Arun K.
; TITLE OF INVENTION: Inhibitors of Memapsin 2 and Use Thereof
; FILE REFERENCE: OMRF 182
; CURRENT APPLICATION NUMBER: US/09/845,226
; CURRENT FILING DATE: 2001-04-30
; PRIOR APPLICATION NUMBER: 09/603,713
; PRIOR FILING DATE: 2000-06-27
; PRIOR APPLICATION NUMBER: 60/168,060
; PRIOR FILING DATE: 1999-11-30
; PRIOR APPLICATION NUMBER: 60/177,836
; PRIOR FILING DATE: 2000-01-25
; PRIOR APPLICATION NUMBER: 60/178,368
; PRIOR FILING DATE: 2000-01-27
; PRIOR APPLICATION NUMBER: 60/210,292
; PRIOR FILING DATE: 2000-06-08
; NUMBER OF SEQ ID NOS: 31
; SOFTWARE: PatentIn Ver. 2.1
; SEQ ID NO 4
;   LENGTH: 10
;   TYPE: PRT
;   ORGANISM: Artificial Sequence
;   FEATURE:
;   OTHER INFORMATION: Description of Artificial Sequence: Primer
US-09-845-226-4

```
Query Match              100.0%;  Score 49;  DB 10;  Length 10;
Best Local Similarity    100.0%;  Pred. No. 0.0017;
Matches   10;  Conservative   0;  Mismatches   0;  Indels   0;  Gaps   0;

Qy       1 SEVKMDAEFR 10
           | | | | | | | | | |
Db       1 SEVKMDAEFR 10


RESULT 9
US-09-795-903A-4
; Sequence 4, Application US/09795903A
; Patent No. US20020164760A1
; GENERAL INFORMATION:
;  APPLICANT: Tang, Jordan J.N.
;  APPLICANT:  Lin, Xinli
;  APPLICANT:  Koelsch, Gerald
;  TITLE OF INVENTION: Catalytically Active Recombinant Memapsin and Methods
;  TITLE OF INVENTION:  of Use Thereof
;  FILE REFERENCE: OMRF 179
;  CURRENT APPLICATION NUMBER: US/09/795,903A
;  CURRENT FILING DATE:  2001-02-28
;  PRIOR APPLICATION NUMBER: 09/604,608
;  PRIOR FILING DATE: 2000-06-27
;  PRIOR APPLICATION NUMBER: 60/168,060
;  PRIOR FILING DATE: 1999-11-30
;  PRIOR APPLICATION NUMBER: 60/177,836
;  PRIOR FILING DATE: 2000-01-25
;  PRIOR APPLICATION NUMBER: 60/178,368
;  PRIOR FILING DATE: 2000-01-27
;  PRIOR APPLICATION NUMBER: 60/210,292
;  PRIOR FILING DATE: 2000-06-08
;  NUMBER OF SEQ ID NOS: 31
;  SOFTWARE: PatentIn Ver. 2.1
; SEQ ID NO 4
;   LENGTH: 10
;   TYPE: PRT
;   ORGANISM: Artificial Sequence
;   FEATURE:
;   OTHER INFORMATION: Description of Artificial Sequence: Primer
US-09-795-903A-4

Query Match              100.0%;  Score 49;  DB 10;  Length 10;
Best Local Similarity    100.0%;  Pred. No. 0.0017;
Matches   10;  Conservative   0;  Mismatches   0;  Indels   0;  Gaps   0;

Qy       1 SEVKMDAEFR 10
           | | | | | | | | | |
Db       1 SEVKMDAEFR 10


RESULT 10
US-09-869-414-64
; Sequence 64, Application US/09869414
; Publication No. US20030077226A1
; GENERAL INFORMATION:
;  APPLICANT: Beinkowski et al.
```

; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR,
AND USES
; TITLE OF INVENTION: THEREFOR
; FILE REFERENCE: 28341/6280M
; CURRENT APPLICATION NUMBER: US/09/869,414
; CURRENT FILING DATE: 2001-06-27
; PRIOR APPLICATION NUMBER: 09/416,901
; PRIOR FILING DATE: 1999-10-13
; PRIOR APPLICATION NUMBER: 60/155,493
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: 09/404,133
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: PCT/US99/20881
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: 60/101,594
; PRIOR FILING DATE: 1998-09-24
; NUMBER OF SEQ ID NOS: 73
; SOFTWARE: PatentIn Ver. 2.0
; SEQ ID NO 64
; LENGTH: 10
; TYPE: PRT
; ORGANISM: Artificial Sequence
; FEATURE:
; OTHER INFORMATION: Description of Artificial Sequence: synthetic
US-09-869-414-64

  Query Match   100.0%; Score 49; DB 11; Length 10;
  Best Local Similarity   100.0%; Pred. No. 0.0017;
  Matches   10; Conservative   0; Mismatches   0; Indels   0; Gaps   0;

Qy   1 SEVKMDAEFR 10
              ||||||||||
Db   1 SEVKMDAEFR 10

RESULT 11
US-09-548-366-64
; Sequence 64, Application US/09548366
; Publication No. US20030104365A1
; GENERAL INFORMATION:
; APPLICANT: Gurney, Mark E.
; APPLICANT: Bienkowski, Michael J.
; APPLICANT: Heinrikson, Robert L.
; APPLICANT: Parodi, Luis A.
; APPLICANT: Yan, Riqiang
; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR,
AND
; TITLE OF INVENTION: USES THEREFOR
; FILE REFERENCE: 28341/6280A
; CURRENT APPLICATION NUMBER: US/09/548,366
; CURRENT FILING DATE: 2000-04-12
; PRIOR APPLICATION NUMBER: 60/155,493
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: 09/404,133
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: PCT/US99/20881
; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: 60/101,594
; PRIOR FILING DATE: 1998-09-24
; NUMBER OF SEQ ID NOS: 65
; SOFTWARE: PatentIn Ver. 2.0
; SEQ ID NO 64
; LENGTH: 10
; TYPE: PRT
; ORGANISM: Artificial Sequence
; FEATURE:
; OTHER INFORMATION: Description of Artificial Sequence: synthetic
US-09-548-366-64

```
  Query Match              100.0%;  Score 49;  DB 11;  Length 10;
  Best Local Similarity    100.0%;  Pred. No. 0.0017;
  Matches   10;  Conservative   0;  Mismatches   0;  Indels   0;  Gaps   0;


Qy          1 SEVKMDAEFR 10
              ||||||||||
Db          1 SEVKMDAEFR 10
```


RESULT 12
US-10-427-208-53
; Sequence 53, Application US/10427208
; Publication No. US20030200555A1
; GENERAL INFORMATION:
; APPLICANT: Merck & Co., Inc.
; APPLICANT: Hazuda, Daria J
; APPLICANT: Chen Dodson, Elizabeth
; APPLICANT: Lai, Ming-Tain
; APPLICANT: Xu, Min
; APPLICANT: Shi, Xiao-Ping
; APPLICANT: Simon, Adam J.
; APPLICANT: Wu, Guoxin
; APPLICANT: Li, Yueming
; APPLICANT: Register, Robert B.
; TITLE OF INVENTION: ASSAYS USING AMYLOID PRECURSOR PROTEINS WITH MODIFIED
; TITLE OF INVENTION: BETA-SECRETASE CLEAVAGE SITES TO MONITOR BETA-SECRETASE
ACTIVITY
; FILE REFERENCE: 21052
; CURRENT APPLICATION NUMBER: US/10/427,208
; CURRENT FILING DATE: 2003-04-30
; NUMBER OF SEQ ID NOS: 75
; SOFTWARE: PatentIn version 3.2
; SEQ ID NO 53
; LENGTH: 10
; TYPE: PRT
; ORGANISM: Homo sapiens
US-10-427-208-53

```
  Query Match              100.0%;  Score 49;  DB 12;  Length 10;
  Best Local Similarity    100.0%;  Pred. No. 0.0017;
  Matches   10;  Conservative   0;  Mismatches   0;  Indels   0;  Gaps   0;


Qy          1 SEVKMDAEFR 10
              ||||||||||
Db          1 SEVKMDAEFR 10
```

RESULT 13
US-10-032-818-7
; Sequence 7, Application US/10032818
; Publication No. US20030092629A1
; GENERAL INFORMATION:
; APPLICANT: Tang, Jordan J.N.
; APPLICANT: Koelsch, Gerald
; APPLICANT: Ghosh, Arun K.
; TITLE OF INVENTION: Inhibitors of Memapsin 2 and Use Thereof
; FILE REFERENCE: 2932.1006-007
; CURRENT APPLICATION NUMBER: US/10/032,818
; CURRENT FILING DATE: 2001-12-28
; PRIOR APPLICATION NUMBER: US 60/275,756
; PRIOR FILING DATE: 2001-03-14
; PRIOR APPLICATION NUMBER: US 60/258,705
; PRIOR FILING DATE: 2000-12-28
; NUMBER OF SEQ ID NOS: 83
; SOFTWARE: FastSEQ for Windows Version 4.0
; SEQ ID NO 7
;   LENGTH: 10
;   TYPE: PRT
;   ORGANISM: Artificial Sequence
;   FEATURE:
;   OTHER INFORMATION: Synthetic peptide
US-10-032-818-7

  Query Match   100.0%; Score 49; DB 15; Length 10;
  Best Local Similarity   100.0%; Pred. No. 0.0017;
  Matches   10; Conservative   0; Mismatches   0; Indels   0; Gaps   0;

Qy   1 SEVKMDAEFR 10
             | | | | | | | | | |
Db   1 SEVKMDAEFR 10

RESULT 14
US-10-354-955-1
; Sequence 1, Application US/10354955
; Publication No. US20030171291A1
; GENERAL INFORMATION:
; APPLICANT: Gary Christie
; APPLICANT: Ishrut Hussain
; APPLICANT: David J. Powell
; TITLE OF INVENTION: No. US20030171291Alel Treatment
; FILE REFERENCE: P32448
; CURRENT APPLICATION NUMBER: US/10/354,955
; CURRENT FILING DATE: 2003-01-30
; PRIOR APPLICATION NUMBER: 09/693,744
; PRIOR FILING DATE: 2000-10-20
; PRIOR APPLICATION NUMBER: 9925136.5
; PRIOR FILING DATE: 1999-10-22
; NUMBER OF SEQ ID NOS: 9
; SOFTWARE: FastSEQ for Windows Version 3.0
; SEQ ID NO 1
;   LENGTH: 11

```
;   TYPE: PRT
;   ORGANISM: human
US-10-354-955-1

   Query Match              100.0%;   Score 49;   DB 12;   Length 11;
   Best Local Similarity    100.0%;   Pred. No. 0.0019;
   Matches   10;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 SEVKMDAEFR 10
              | | | | | | | | | |
Db          2 SEVKMDAEFR 11


RESULT 15
US-10-354-955-3
; Sequence 3, Application US/10354955
; Publication No. US20030171291A1
; GENERAL INFORMATION:
;  APPLICANT: Gary Christie
;  APPLICANT:  Ishrut Hussain
;  APPLICANT:  David J. Powell
;  TITLE OF INVENTION: No. US20030171291A1el Treatment
;  FILE REFERENCE: P32448
;  CURRENT APPLICATION NUMBER: US/10/354,955
;  CURRENT FILING DATE:  2003-01-30
;  PRIOR APPLICATION NUMBER: 09/693,744
;  PRIOR FILING DATE: 2000-10-20
;  PRIOR APPLICATION NUMBER: 9925136.5
;  PRIOR FILING DATE: 1999-10-22
;  NUMBER OF SEQ ID NOS: 9
;  SOFTWARE: FastSEQ for Windows Version 3.0
; SEQ ID NO 3
;   LENGTH: 11
;   TYPE: PRT
;   ORGANISM: Artificial Sequence
;   FEATURE:
;   OTHER INFORMATION: fusion protein with maltose binding protein attached at
residue 1'
US-10-354-955-3

   Query Match              100.0%;   Score 49;   DB 12;   Length 11;
   Best Local Similarity    100.0%;   Pred. No. 0.0019;
   Matches   10;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 SEVKMDAEFR 10
              | | | | | | | | | |
Db          2 SEVKMDAEFR 11


Search completed: January 21, 2004, 09:41:42
Job time : 3.00765 secs
```

GenCore version 5.1.6
Copyright (c) 1993 - 2004 Compugen Ltd.

OM protein - protein search, using sw model

Run on: January 21, 2004, 09:16:19 ; Search time 2.06501 Seconds
                                             (without alignments)
                                             1249.644 Million cell updates/sec

Title: US-09-869-414A-64
Perfect score: 49
Sequence: 1 SEVKMDAEFR 10

Scoring table: BLOSUM62
                 Gapop 10.0 , Gapext 0.5

Searched: 830525 seqs, 258052604 residues

Total number of hits satisfying chosen parameters: 830525

Minimum DB seq length: 0
Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%
                 Maximum Match 100%
                 Listing first 45 summaries

Database :   SPTREMBL_23:*
                 1:   sp_archea:*
                 2:   sp_bacteria:*
                 3:   sp_fungi:*
                 4:   sp_human:*
                 5:   sp_invertebrate:*
                 6:   sp_mammal:*
                 7:   sp_mhc:*
                 8:   sp_organelle:*
                 9:   sp_phage:*
                 10: sp_plant:*
                 11: sp_rodent:*
                 12: sp_virus:*
                 13: sp_vertebrate:*
                 14: sp_unclassified:*
                 15: sp_rvirus:*
                 16: sp_bacteriap:*
                 17: sp_archeap:*

        Pred. No. is the number of results predicted by chance to have a
        score greater than or equal to the score of the result being printed,
        and is derived by analysis of the total score distribution.

                                SUMMARIES
                      %
Result   Query
   No.   Score   Match Length DB   ID   Description

1	49	100.0	35	4	Q8WZ99	Q8wz99 homo sapien
2	49	100.0	82	4	Q16020	Q16020 homo sapien
3	49	100.0	82	4	Q16014	Q16014 homo sapien
4	49	100.0	82	4	Q16019	Q16019 homo sapien
5	49	100.0	113	13	Q8JH58	Q8jh58 chelydra se
6	49	100.0	534	13	O93296	O93296 gallus gall
7	49	100.0	569	13	Q9PVL1	Q9pvl1 gallus gall
8	49	100.0	695	11	Q60496	Q60496 cavia sp. p
9	49	100.0	695	13	Q9DGJ8	Q9dgj8 gallus gall
10	49	100.0	751	13	Q9DGJ7	Q9dgj7 gallus gall
11	49	100.0	770	6	Q9TUI0	Q9tui0 sus scrofa
12	44	89.8	79	11	O35463	O35463 cricetulus
13	44	89.8	218	11	Q8BPV5	Q8bpv5 mus musculu
14	44	89.8	384	11	Q8BPC7	Q8bpc7 mus musculu
15	44	89.8	607	11	Q99K32	Q99k32 mus musculu
16	44	89.8	695	11	P97487	P97487 mus musculu
17	43	87.8	693	13	Q98SG0	Q98sg0 xenopus lae
18	43	87.8	695	13	Q98SF9	Q98sf9 xenopus lae
19	43	87.8	747	13	Q91963	Q91963 xenopus. ap
20	42	85.7	423	2	O52379	O52379 ralstonia s
21	42	85.7	423	2	Q45693	Q45693 burkholderi
22	39	79.6	142	5	O16896	O16896 caenorhabdi
23	36	73.5	630	2	Q93IK4	Q93ik4 vibrio sp.
24	35	71.4	317	17	Q96ZT2	Q96zt2 sulfolobus
25	35	71.4	419	2	Q8GHI9	Q8ghi9 pigmentipha
26	35	71.4	774	16	Q92CV7	Q92cv7 listeria in
27	35	71.4	2148	5	Q8IPL5	Q8ipl5 drosophila
28	34	69.4	239	10	Q9FNG2	Q9fng2 arabidopsis
29	34	69.4	254	5	Q8IK90	Q8ik90 plasmodium
30	34	69.4	605	16	Q9L1F6	Q9l1f6 streptomyce
31	34	69.4	626	16	Q8ZCN4	Q8zcn4 yersinia pe
32	34	69.4	1192	10	Q94BS1	Q94bs1 arabidopsis
33	34	69.4	1261	10	Q9LU30	Q9lu30 arabidopsis
34	34	69.4	3262	4	Q13788	Q13788 homo sapien
35	33	67.3	302	9	Q37840	Q37840 bacteriopha
36	33	67.3	438	2	Q9AIK4	Q9aik4 bilophila w
37	33	67.3	449	16	Q8D1Z2	Q8d1z2 wiggleswort
38	33	67.3	582	16	Q8KFP0	Q8kfp0 chlorobium
39	33	67.3	621	4	Q9H9Y1	Q9h9y1 homo sapien
40	33	67.3	711	16	Q8EFW4	Q8efw4 shewanella
41	33	67.3	1027	4	Q9BWX2	Q9bwx2 homo sapien
42	33	67.3	1245	10	Q9C7F8	Q9c7f8 arabidopsis
43	32	65.3	143	4	Q9H935	Q9h935 homo sapien
44	32	65.3	161	16	Q98FZ2	Q98fz2 rhizobium l
45	32	65.3	286	2	Q8VNV1	Q8vnv1 chlorobium

ALIGNMENTS

RESULT 1
Q8WZ99
ID   Q8WZ99   PRELIMINARY;   PRT;   35 AA.
AC   Q8WZ99;
DT   01-MAR-2002 (TrEMBLrel. 20, Created)
DT   01-MAR-2002 (TrEMBLrel. 20, Last sequence update)
DT   01-MAR-2002 (TrEMBLrel. 20, Last annotation update)

DE   Amyloid protein (Fragment).
GN   APP.
OS   Homo sapiens (Human).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC   Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
OX   NCBI_TaxID=9606;
RN   [1]
RP   SEQUENCE FROM N.A.
RA   Wakutani Y., Ninomiya H., Iwata H., Tanaka S., Urakami K., Adachi Y.,
RA   Wada-Isoe K., Yamagata K., Ohono K., Tsubuki S., Saido T.,
RA   Hashimoto T., Iwatsubo T., Nakashima K.;
RT   "Novel missense mutation (D678N) of amyloid precursor protein gene in
RT   a Japanese pedigree of familial Alzheimer's disease.";
RL   Submitted (JUL-2001) to the EMBL/GenBank/DDBJ databases.
DR   EMBL; AB066441; BAB71958.1; -.
FT   NON_TER   1   1
FT   NON_TER   35   35
SQ   SEQUENCE   35 AA;   4084 MW;   49D7D17289743B71 CRC64;

   Query Match   100.0%;   Score 49;   DB 4;   Length 35;
   Best Local Similarity   100.0%;   Pred. No. 0.0045;
   Matches   10; Conservative   0; Mismatches   0; Indels   0; Gaps   0;

Qy   1 SEVKMDAEFR 10
             ||||||||||
Db   12 SEVKMDAEFR 21

RESULT 2
Q16020
ID   Q16020   PRELIMINARY;   PRT;   82 AA.
AC   Q16020;
DT   01-NOV-1996 (TrEMBLrel. 01, Created)
DT   01-NOV-1996 (TrEMBLrel. 01, Last sequence update)
DT   01-JUN-2002 (TrEMBLrel. 21, Last annotation update)
DE   Beta-amyloid peptide (Fragment).
GN   BETA APP.
OS   Homo sapiens (Human).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC   Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
OX   NCBI_TaxID=9606;
RN   [1]
RP   SEQUENCE FROM N.A.
RX   MEDLINE=93236601; PubMed=8476439;
RA   Denman R.B., Rosenzcwaig R., Miller D.L.;
RT   "A system for studying the effect(s) of familial Alzheimer disease
RT   mutations on the processing of the beta-amyloid peptide precursor.";
RL   Biochem. Biophys. Res. Commun. 192:96-103(1993).
DR   EMBL; S61383; AAB26265.2; -.
DR   HSSP; P05067; 1BA4.
DR   InterPro; IPR001255; Beta-APP.
DR   Pfam; PF03494; Beta-APP; 1.
FT   NON_TER   1   1
FT   NON_TER   82   82
SQ   SEQUENCE   82 AA;   8882 MW;   F534AA5AE5D9230A CRC64;

   Query Match   100.0%;   Score 49;   DB 4;   Length 82;

```
      Best Local Similarity   100.0%;  Pred. No. 0.011;
      Matches   10;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy           1 SEVKMDAEFR 10
               ||||||||||
Db          13 SEVKMDAEFR 22
```

RESULT 3
Q16014
```
ID   Q16014      PRELIMINARY;      PRT;    82 AA.
AC   Q16014;
DT   01-NOV-1996 (TrEMBLrel. 01, Created)
DT   01-NOV-1996 (TrEMBLrel. 01, Last sequence update)
DT   01-JUN-2002 (TrEMBLrel. 21, Last annotation update)
DE   Beta-amyloid peptide (Fragment).
OS   Homo sapiens (Human).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC   Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
OX   NCBI_TaxID=9606;
RN   [1]
RP   SEQUENCE FROM N.A.
RX   MEDLINE=93236601; PubMed=8476439;
RA   Denman R.B., Rosenzcwaig R., Miller D.L.;
RT   "A system for studying the effect(s) of familial Alzheimer disease
RT   mutations on the processing of the beta-amyloid peptide precursor.";
RL   Biochem. Biophys. Res. Commun. 192:96-103(1993).
DR   EMBL; S60721; AAB26263.2; -.
DR   HSSP; P05067; 1BA4.
DR   InterPro; IPR001255; Beta-APP.
DR   Pfam; PF03494; Beta-APP; 1.
FT   NON_TER       1      1
FT   NON_TER      82     82
SQ   SEQUENCE    82 AA;  8972 MW;   F534AA5B3EA9230A CRC64;
```

```
   Query Match              100.0%;  Score 49;  DB 4;  Length 82;
   Best Local Similarity   100.0%;  Pred. No. 0.011;
   Matches   10;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy           1 SEVKMDAEFR 10
               ||||||||||
Db          13 SEVKMDAEFR 22
```

RESULT 4
Q16019
```
ID   Q16019      PRELIMINARY;      PRT;    82 AA.
AC   Q16019;
DT   01-NOV-1996 (TrEMBLrel. 01, Created)
DT   01-NOV-1996 (TrEMBLrel. 01, Last sequence update)
DT   01-JUN-2002 (TrEMBLrel. 21, Last annotation update)
DE   Beta-amyloid peptide (Fragment).
GN   BETA APP.
OS   Homo sapiens (Human).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC   Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
OX   NCBI_TaxID=9606;
```

RN   [1]
RP   SEQUENCE FROM N.A.
RX   MEDLINE=93236601; PubMed=8476439;
RA   Denman R.B., Rosenzcwaig R., Miller D.L.;
RT   "A system for studying the effect(s) of familial Alzheimer disease
RT   mutations on the processing of the beta-amyloid peptide precursor.";
RL   Biochem. Biophys. Res. Commun. 192:96-103(1993).
DR   EMBL; S61380; AAB26264.2; -.
DR   HSSP; P05067; 1BA4.
DR   InterPro; IPR001255; Beta-APP.
DR   Pfam; PF03494; Beta-APP; 1.
FT   NON_TER   1   1
FT   NON_TER   82   82
SQ   SEQUENCE   82 AA;   8938 MW;   F534AA50E579230A CRC64;

    Query Match   100.0%;   Score 49;   DB 4;   Length 82;
    Best Local Similarity   100.0%;   Pred. No. 0.011;
    Matches   10;   Conservative   0;   Mismatches   0;   Indels   0;   Gaps   0;

Qy   1 SEVKMDAEFR 10
               ||||||||||
Db   13 SEVKMDAEFR 22

RESULT 5
Q8JH58
ID   Q8JH58   PRELIMINARY;   PRT;   113 AA.
AC   Q8JH58;
DT   01-OCT-2002 (TrEMBLrel. 22, Created)
DT   01-OCT-2002 (TrEMBLrel. 22, Last sequence update)
DT   01-MAR-2003 (TrEMBLrel. 23, Last annotation update)
DE   Amyloid beta protein (Fragment).
OS   Chelydra serpentina serpentina (common snapping turtle).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC   Testudines; Cryptodira; Testudinoidea; Chelydridae; Chelydra.
OX   NCBI_TaxID=134619;
RN   [1]
RP   SEQUENCE FROM N.A.
RX   MEDLINE=21876906; PubMed=11882478;
RA   Trudeau V.L., Chiu S., Kennedy S.W., Brooks R.J.;
RT   "Octylphenol (OP) alters the expression of members of the amyloid
RT   protein family in the hypothalamus of the snapping turtle, Chelydra
RT   serpentina serpentina.";
RL   Environ. Health Perspect. 110:269-275(2002).
DR   EMBL; AF541917; AAN04908.1; -.
DR   InterPro; IPR001868; A4_APP.
DR   InterPro; IPR001255; Beta-APP.
DR   Pfam; PF03494; Beta-APP; 1.
DR   PRINTS; PR00203; AMYLOIDA4.
DR   PROSITE; PS00320; A4_INTRA; 1.
FT   NON_TER   1   1
SQ   SEQUENCE   113 AA;   12750 MW;   72515C930496E053 CRC64;

    Query Match   100.0%;   Score 49;   DB 13;   Length 113;
    Best Local Similarity   100.0%;   Pred. No. 0.015;
    Matches   10;   Conservative   0;   Mismatches   0;   Indels   0;   Gaps   0;

```
Qy          1 SEVKMDAEFR 10
              | | | | | | | | | |
Db         10 SEVKMDAEFR 19
```

RESULT 6
O93296
```
ID   O93296        PRELIMINARY;        PRT;    534 AA.
AC   O93296;
DT   01-NOV-1998 (TrEMBLrel. 08, Created)
DT   01-NOV-1998 (TrEMBLrel. 08, Last sequence update)
DT   01-OCT-2002 (TrEMBLrel. 22, Last annotation update)
DE   Amyloid protein (Fragment).
OS   Gallus gallus (Chicken).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC   Archosauria; Aves; Neognathae; Galliformes; Phasianidae; Phasianinae;
OC   Gallus.
OX   NCBI_TaxID=9031;
RN   [1]
RP   SEQUENCE FROM N.A.
RX   MEDLINE=98337885; PubMed=9671674;
RA   Barnes N.Y., Li L., Yoshikawa K., Schwartz L.M., Oppenheim R.W.,
RA   Milligan C.E.;
RT   "Increased production of amyloid precursor protein provides a
RT   substrate for caspase-3 in dying motoneurons.";
RL   J. Neurosci. 18:5869-5880(1998).
DR   EMBL; AF042098; AAC25052.1; -.
DR   HSSP; P05067; 1BA4.
DR   InterPro; IPR001868; A4_APP.
DR   InterPro; IPR001255; Beta-APP.
DR   Pfam; PF02177; A4_EXTRA; 1.
DR   Pfam; PF03494; Beta-APP; 1.
DR   PRINTS; PR00203; AMYLOIDA4.
DR   PROSITE; PS00319; A4_EXTRA; 1.
DR   PROSITE; PS00320; A4_INTRA; 1.
FT   NON_TER        1        1
SQ   SEQUENCE    534 AA;    60597 MW;    FB53ECC2E66D4C92 CRC64;
```

```
   Query Match                100.0%;   Score 49;   DB 13;   Length 534;
   Best Local Similarity    100.0%;   Pred. No. 0.075;
   Matches    10;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;
```

```
Qy          1 SEVKMDAEFR 10
              | | | | | | | | | |
Db        431 SEVKMDAEFR 440
```

RESULT 7
Q9PVL1
```
ID   Q9PVL1        PRELIMINARY;        PRT;    569 AA.
AC   Q9PVL1;
DT   01-MAY-2000 (TrEMBLrel. 13, Created)
DT   01-MAY-2000 (TrEMBLrel. 13, Last sequence update)
DT   01-MAR-2003 (TrEMBLrel. 23, Last annotation update)
DE   Amyloid protein (Fragment).
GN   APP.
OS   Gallus gallus (Chicken).
```

OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC   Archosauria; Aves; Neognathae; Galliformes; Phasianidae; Phasianinae;
OC   Gallus.
OX   NCBI_TaxID=9031;
RN   [1]
RP   SEQUENCE FROM N.A.
RC   TISSUE=Brain;
RA   Coulson E.J., Paliga K., Beyreuther K., Masters C.L.;
RT   "What the evolution of the amyloid protein precursor supergene family
RT   tells us about its function.";
RL   Neurochem. Int. 0:0-0(2000).
DR   EMBL; AF030341; AAF12698.1; -.
DR   HSSP; P05067; 1BA4.
DR   InterPro; IPR001868; A4_APP.
DR   InterPro; IPR001255; Beta-APP.
DR   Pfam; PF02177; A4_EXTRA; 1.
DR   Pfam; PF03494; Beta-APP; 1.
DR   PRINTS; PR00203; AMYLOIDA4.
DR   PROSITE; PS00319; A4_EXTRA; 1.
DR   PROSITE; PS00320; A4_INTRA; 1.
FT   NON_TER   1   1
SQ   SEQUENCE   569 AA;   64753 MW;   0AB8BB851863A19D CRC64;

    Query Match   100.0%;   Score 49;   DB 13;   Length 569;
    Best Local Similarity   100.0%;   Pred. No. 0.08;
    Matches   10;   Conservative   0;   Mismatches   0;   Indels   0;   Gaps   0;

Qy   1 SEVKMDAEFR 10
             ||||||||||
Db   467 SEVKMDAEFR 476

RESULT 8
Q60496
ID   Q60496   PRELIMINARY;   PRT;   695 AA.
AC   Q60496;
DT   01-NOV-1996 (TrEMBLrel. 01, Created)
DT   01-NOV-1996 (TrEMBLrel. 01, Last sequence update)
DT   01-OCT-2002 (TrEMBLrel. 22, Last annotation update)
DE   Putative amyloid precursor protein.
OS   Cavia sp.
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC   Mammalia; Eutheria; Rodentia; Hystricognathi; Caviidae; Cavia.
OX   NCBI_TaxID=10143;
RN   [1]
RP   SEQUENCE FROM N.A.
RC   TISSUE=Brain;
RX   MEDLINE=97236426; PubMed=9116031;
RA   Beck M., Mueller D., Bigl V.;
RT   "Amyloid precursor protein in Guinea pigs - complete cDNA sequence and
RT   alternative splicing.";
RL   Biochim. Biophys. Acta 1351:17-21(1997).
DR   EMBL; X97631; CAA66230.1; -.
DR   HSSP; P05067; 1BA4.
DR   InterPro; IPR001868; A4_APP.
DR   InterPro; IPR001255; Beta-APP.
DR   Pfam; PF02177; A4_EXTRA; 1.

```
DR    Pfam; PF03494; Beta-APP; 1.
DR    PRINTS; PR00203; AMYLOIDA4.
DR    SMART; SM00006; A4_EXTRA; 1.
DR    PROSITE; PS00319; A4_EXTRA; 1.
DR    PROSITE; PS00320; A4_INTRA; 1.
SQ    SEQUENCE   695 AA;  78701 MW;  5196A0C4017F16AB CRC64;

   Query Match              100.0%;  Score 49;  DB 11;  Length 695;
   Best Local Similarity   100.0%;  Pred. No. 0.099;
   Matches   10;  Conservative   0;  Mismatches   0;  Indels   0;  Gaps   0;

Qy         1 SEVKMDAEFR 10
             ||||||||||
Db       592 SEVKMDAEFR 601


RESULT 9
Q9DGJ8
ID    Q9DGJ8        PRELIMINARY;        PRT;    695 AA.
AC    Q9DGJ8;
DT    01-MAR-2001 (TrEMBLrel. 16, Created)
DT    01-MAR-2001 (TrEMBLrel. 16, Last sequence update)
DT    01-OCT-2002 (TrEMBLrel. 22, Last annotation update)
DE    Beta-amyloid precursor protein 695 isoform.
OS    Gallus gallus (Chicken).
OC    Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC    Archosauria; Aves; Neognathae; Galliformes; Phasianidae; Phasianinae;
OC    Gallus.
OX    NCBI_TaxID=9031;
RN    [1]
RP    SEQUENCE FROM N.A.
RA    Sarasa M., Rodolosse A., Sorribas V.;
RT    "Cloning of full-length chicken beta-amyloid precursor protein
RT    isoforms.";
RL    Submitted (JUL-2000) to the EMBL/GenBank/DDBJ databases.
DR    EMBL; AF289218; AAG00593.1; -.
DR    HSSP; P05067; 1BA4.
DR    InterPro; IPR001868; A4_APP.
DR    InterPro; IPR001255; Beta-APP.
DR    Pfam; PF02177; A4_EXTRA; 1.
DR    Pfam; PF03494; Beta-APP; 1.
DR    PRINTS; PR00203; AMYLOIDA4.
DR    SMART; SM00006; A4_EXTRA; 1.
DR    PROSITE; PS00319; A4_EXTRA; 1.
DR    PROSITE; PS00320; A4_INTRA; 1.
SQ    SEQUENCE   695 AA;  78565 MW;  F201ED02AEC86D95 CRC64;

   Query Match              100.0%;  Score 49;  DB 13;  Length 695;
   Best Local Similarity   100.0%;  Pred. No. 0.099;
   Matches   10;  Conservative   0;  Mismatches   0;  Indels   0;  Gaps   0;

Qy         1 SEVKMDAEFR 10
             ||||||||||
Db       592 SEVKMDAEFR 601


RESULT 10
```

Q9DGJ7
```
ID   Q9DGJ7        PRELIMINARY;        PRT;    751 AA.
AC   Q9DGJ7;
DT   01-MAR-2001 (TrEMBLrel. 16, Created)
DT   01-MAR-2001 (TrEMBLrel. 16, Last sequence update)
DT   01-OCT-2002 (TrEMBLrel. 22, Last annotation update)
DE   Beta-amyloid precursor protein 751 isoform.
OS   Gallus gallus (Chicken).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC   Archosauria; Aves; Neognathae; Galliformes; Phasianidae; Phasianinae;
OC   Gallus.
OX   NCBI_TaxID=9031;
RN   [1]
RP   SEQUENCE FROM N.A.
RA   Sarasa M., Rodolosse A., Sorribas V.;
RT   "Cloning of full-length chicken beta-amyloid precursor protein
RT   isoforms.";
RL   Submitted (JUL-2000) to the EMBL/GenBank/DDBJ databases.
DR   EMBL; AF289219; AAG00594.1; -.
DR   HSSP; P05067; 1BA4.
DR   InterPro; IPR001868; A4_APP.
DR   InterPro; IPR001255; Beta-APP.
DR   InterPro; IPR002223; Kunitz_BPTI.
DR   Pfam; PF02177; A4_EXTRA; 1.
DR   Pfam; PF03494; Beta-APP; 1.
DR   Pfam; PF00014; Kunitz_BPTI; 1.
DR   PRINTS; PR00203; AMYLOIDA4.
DR   PRINTS; PR00759; BASICPTASE.
DR   ProDom; PD000222; Kunitz_BPTI; 1.
DR   SMART; SM00006; A4_EXTRA; 1.
DR   SMART; SM00131; KU; 1.
DR   PROSITE; PS00319; A4_EXTRA; 1.
DR   PROSITE; PS00320; A4_INTRA; 1.
DR   PROSITE; PS00280; BPTI_KUNITZ_1; 1.
DR   PROSITE; PS50279; BPTI_KUNITZ_2; 1.
KW   Protease inhibitor; Serine protease inhibitor.
SQ   SEQUENCE   751 AA;   84705 MW;   E78E9413A8033D84 CRC64;
```

```
   Query Match              100.0%;  Score 49;  DB 13;  Length 751;
   Best Local Similarity    100.0%;  Pred. No. 0.11;
   Matches    10;  Conservative     0;  Mismatches     0;  Indels    0;  Gaps    0;

Qy          1 SEVKMDAEFR 10
               ||||||||||
Db        648 SEVKMDAEFR 657
```

RESULT 11
Q9TUI0
```
ID   Q9TUI0        PRELIMINARY;        PRT;    770 AA.
AC   Q9TUI0;
DT   01-MAY-2000 (TrEMBLrel. 13, Created)
DT   01-MAY-2000 (TrEMBLrel. 13, Last sequence update)
DT   01-OCT-2002 (TrEMBLrel. 22, Last annotation update)
DE   Amyloid precursor protein.
OS   Sus scrofa (Pig).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
```

```
OC    Mammalia; Eutheria; Cetartiodactyla; Suina; Suidae; Sus.
OX    NCBI_TaxID=9823;
RN    [1]
RP    SEQUENCE FROM N.A.
RA    Kimura A., Takahashi T.;
RT    "Amyloid Precursor Protein 770.";
RL    Submitted (SEP-1999) to the EMBL/GenBank/DDBJ databases.
DR    EMBL; AB032550; BAA84580.1; -.
DR    HSSP; P05067; 1AAP.
DR    InterPro; IPR001868; A4_APP.
DR    InterPro; IPR001255; Beta-APP.
DR    InterPro; IPR002223; Kunitz_BPTI.
DR    Pfam; PF02177; A4_EXTRA; 1.
DR    Pfam; PF03494; Beta-APP; 1.
DR    Pfam; PF00014; Kunitz_BPTI; 1.
DR    PRINTS; PR00203; AMYLOIDA4.
DR    PRINTS; PR00759; BASICPTASE.
DR    ProDom; PD000222; Kunitz_BPTI; 1.
DR    SMART; SM00006; A4_EXTRA; 1.
DR    SMART; SM00131; KU; 1.
DR    PROSITE; PS00319; A4_EXTRA; 1.
DR    PROSITE; PS00320; A4_INTRA; 1.
DR    PROSITE; PS00280; BPTI_KUNITZ_1; 1.
DR    PROSITE; PS50279; BPTI_KUNITZ_2; 1.
KW    Protease inhibitor; Serine protease inhibitor.
SQ    SEQUENCE    770 AA;    86961 MW;    5F7A1DCB2BCC583E CRC64;

   Query Match              100.0%;  Score 49;  DB 6;  Length 770;
   Best Local Similarity    100.0%;  Pred. No. 0.11;
   Matches    10;  Conservative     0;  Mismatches     0;  Indels     0;  Gaps     0;


Qy           1 SEVKMDAEFR 10
               ||||||||||
Db         667 SEVKMDAEFR 676



RESULT 12
O35463
ID    O35463        PRELIMINARY;      PRT;      79 AA.
AC    O35463;
DT    01-JAN-1998 (TrEMBLrel. 05, Created)
DT    01-JAN-1998 (TrEMBLrel. 05, Last sequence update)
DT    01-JUN-2002 (TrEMBLrel. 21, Last annotation update)
DE    Alzheimer's amyloid beta protein (Fragment).
GN    BETA APP.
OS    Cricetulus griseus (Chinese hamster).
OC    Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC    Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Cricetinae;
OC    Cricetulus.
OX    NCBI_TaxID=10029;
RN    [1]
RP    SEQUENCE FROM N.A.
RA    Sambamurti K., Pinnix I., Gandhi S.;
RL    Submitted (OCT-1997) to the EMBL/GenBank/DDBJ databases.
DR    EMBL; AF030413; AAB86608.1; -.
DR    HSSP; P05067; 1BA4.
DR    InterPro; IPR001255; Beta-APP.
```

```
DR    Pfam; PF03494; Beta-APP; 1.
FT    NON_TER          1         1
FT    NON_TER         79        79
SQ    SEQUENCE    79 AA;   8538 MW;   37F2C6C3BFF3F597 CRC64;

   Query Match                89.8%;   Score 44;   DB 11;   Length 79;
   Best Local Similarity   100.0%;   Pred. No. 0.12;
   Matches     9;   Conservative     0;   Mismatches     0;   Indels     0;   Gaps     0;


Qy            1 SEVKMDAEF 9
                IIIIIIIII
Db           16 SEVKMDAEF 24



RESULT 13
Q8BPV5
ID    Q8BPV5        PRELIMINARY;        PRT;    218 AA.
AC    Q8BPV5;
DT    01-MAR-2003 (TrEMBLrel. 23, Created)
DT    01-MAR-2003 (TrEMBLrel. 23, Last sequence update)
DT    01-MAR-2003 (TrEMBLrel. 23, Last annotation update)
DE    Amyloid beta (Fragment).
OS    Mus musculus (Mouse).
OC    Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC    Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Mus.
OX    NCBI_TaxID=10090;
RN    [1]
RP    SEQUENCE FROM N.A.
RC    STRAIN=C57BL/6J; TISSUE=Lung;
RX    MEDLINE=22354683; PubMed=12466851;
RA    The FANTOM Consortium,
RA    the RIKEN Genome Exploration Research Group Phase I & II Team;
RT    "Analysis of the mouse transcriptome based on functional annotation of
RT    60,770 full-length cDNAs.";
RL    Nature 420:563-573(2002).
DR    EMBL; AK052448; BAC34997.1; -.
FT    NON_TER          1         1
SQ    SEQUENCE   218 AA;   24118 MW;   95B55AFDAE1D0EF5 CRC64;

   Query Match                89.8%;   Score 44;   DB 11;   Length 218;
   Best Local Similarity   100.0%;   Pred. No. 0.34;
   Matches     9;   Conservative     0;   Mismatches     0;   Indels     0;   Gaps     0;


Qy            1 SEVKMDAEF 9
                IIIIIIIII
Db          115 SEVKMDAEF 123



RESULT 14
Q8BPC7
ID    Q8BPC7        PRELIMINARY;        PRT;    384 AA.
AC    Q8BPC7;
DT    01-MAR-2003 (TrEMBLrel. 23, Created)
DT    01-MAR-2003 (TrEMBLrel. 23, Last sequence update)
DT    01-MAR-2003 (TrEMBLrel. 23, Last annotation update)
DE    Amyloid beta (Fragment).
OS    Mus musculus (Mouse).
```

```
OC    Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC    Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Mus.
OX    NCBI_TaxID=10090;
RN    [1]
RP    SEQUENCE FROM N.A.
RC    STRAIN=C57BL/6J; TISSUE=Head;
RX    MEDLINE=22354683; PubMed=12466851;
RA    The FANTOM Consortium,
RA    the RIKEN Genome Exploration Research Group Phase I & II Team;
RT    "Analysis of the mouse transcriptome based on functional annotation of
RT    60,770 full-length cDNAs.";
RL    Nature 420:563-573(2002).
DR    EMBL; AK076506; BAC36369.1; -.
FT    NON_TER          1        1
SQ    SEQUENCE    384 AA;    43990 MW;    A81B1AD8AE683173 CRC64;
```

```
  Query Match                89.8%;  Score 44;  DB 11;  Length 384;
  Best Local Similarity    100.0%;  Pred. No. 0.61;
  Matches      9;  Conservative     0;  Mismatches     0;  Indels     0;  Gaps     0;


Qy           1 SEVKMDAEF 9
               |||||||||
Db         281 SEVKMDAEF 289
```

```
RESULT 15
Q99K32
ID    Q99K32        PRELIMINARY;      PRT;     607 AA.
AC    Q99K32;
DT    01-JUN-2001 (TrEMBLrel. 17, Created)
DT    01-JUN-2001 (TrEMBLrel. 17, Last sequence update)
DT    01-OCT-2002 (TrEMBLrel. 22, Last annotation update)
DE    Hypothetical 68.4 kDa protein (Fragment).
GN    APP.
OS    Mus musculus (Mouse).
OC    Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC    Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Mus.
OX    NCBI_TaxID=10090;
RN    [1]
RP    SEQUENCE FROM N.A.
RA    Strausberg R.;
RL    Submitted (MAR-2001) to the EMBL/GenBank/DDBJ databases.
DR    EMBL; BC005490; AAH05490.1; -.
DR    HSSP; P05067; 1AAP.
DR    MGD; MGI:88059; App.
DR    InterPro; IPR001868; A4_APP.
DR    InterPro; IPR001255; Beta-APP.
DR    InterPro; IPR002223; Kunitz_BPTI.
DR    Pfam; PF02177; A4_EXTRA; 1.
DR    Pfam; PF03494; Beta-APP; 1.
DR    Pfam; PF00014; Kunitz_BPTI; 1.
DR    PRINTS; PR00203; AMYLOIDA4.
DR    PRINTS; PR00759; BASICPTASE.
DR    ProDom; PD000222; Kunitz_BPTI; 1.
DR    SMART; SM00131; KU; 1.
DR    PROSITE; PS00319; A4_EXTRA; 1.
DR    PROSITE; PS00320; A4_INTRA; 1.
```

```
DR    PROSITE; PS00280; BPTI_KUNITZ_1; 1.
DR    PROSITE; PS50279; BPTI_KUNITZ_2; 1.
KW    Hypothetical protein; Protease inhibitor; Serine protease inhibitor.
FT    NON_TER        1        1
SQ    SEQUENCE    607 AA;   68391 MW;   BF802214CBA7D172 CRC64;

   Query Match              89.8%;  Score 44;  DB 11;  Length 607;
   Best Local Similarity   100.0%;  Pred. No. 0.98;
   Matches    9;  Conservative   0;  Mismatches   0;  Indels   0;  Gaps   0;

Qy         1 SEVKMDAEF 9
             |||||||||
Db       504 SEVKMDAEF 512


Search completed: January 21, 2004, 09:25:08
Job time : 3.06501 secs
```

GenCore version 5.1.6
Copyright (c) 1993 - 2004 Compugen Ltd.

OM protein - protein search, using sw model

Run on: January 21, 2004, 09:15:44 ; Search time 0.497132 Seconds
                                               (without alignments)
                                               945.960 Million cell updates/sec

Title: US-09-869-414A-64
Perfect score: 49
Sequence: 1 SEVKMDAEFR 10

Scoring table: BLOSUM62
                   Gapop 10.0 , Gapext 0.5

Searched: 127863 seqs, 47026705 residues

Total number of hits satisfying chosen parameters: 127863

Minimum DB seq length: 0
Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%
                 Maximum Match 100%
                 Listing first 45 summaries

Database :   SwissProt_41:*

        Pred. No. is the number of results predicted by chance to have a
        score greater than or equal to the score of the result being printed,
        and is derived by analysis of the total score distribution.

                                  SUMMARIES
                    %
Result   Query
   No.   Score   Match Length DB   ID   Description
----
     1   49   100.0   57   1   A4_URSMA   Q29149 ursus marit
     2   49   100.0   58   1   A4_CANFA   Q28280 canis famil
     3   49   100.0   58   1   A4_RABIT   Q28748 oryctolagus
     4   49   100.0   58   1   A4_SHEEP   Q28757 ovis aries
     5   49   100.0   59   1   A4_BOVIN   Q28053 bos taurus
     6   49   100.0   751   1   A4_SAISC   Q95241 s amyloid b
     7   49   100.0   770   1   A4_CAVPO   Q60495 c amyloid b
     8   49   100.0   770   1   A4_HUMAN   P05067 h amyloid b
     9   49   100.0   770   1   A4_MACFA   P53601 m amyloid b
    10   49   100.0   770   1   A4_PIG   P79307 s amyloid b
    11   44   89.8   770   1   A4_MOUSE   P12023 m amyloid b
    12   44   89.8   770   1   A4_RAT   P08592 r amyloid b
    13   37   75.5   269   1   T2S1_STRFI   O52512 streptomyce
    14   34   69.4   3562   1   PGCV_CHICK   Q90953 gallus gall
    15   34   69.4   4563   1   APB_HUMAN   P04114 homo sapien
    16   33   67.3   927   1   CC15_SCHPO   Q09822 schizosacch
    17   32   65.3   263   1   Y683_HALN1   Q9hri2 halobacteri

18	32	65.3	354	1	BCPA_CHLLT	Q46135	chlorobium
19	32	65.3	365	1	BCPA_CHLTE	Q46393	chlorobium
20	32	65.3	776	1	OSTA_VIBVU	Q8ded5	vibrio vuln
21	32	65.3	1906	1	YFA0_ANASP	Q8ym40	anabaena sp
22	31	63.3	81	1	RS16_CLOPE	Q8xjp4	clostridium
23	31	63.3	178	1	YJGA_HAEIN	P45076	haemophilus
24	31	63.3	183	1	YJGA_ECOLI	P26650	escherichia
25	31	63.3	198	1	TNF4_MOUSE	P43488	mus musculu
26	31	63.3	279	1	RFA2_SCHPO	Q92373	schizosacch
27	31	63.3	346	1	PA6A_HUMAN	Q9npb6	homo sapien
28	31	63.3	346	1	PA6A_MOUSE	Q9z101	mus musculu
29	31	63.3	416	1	TRPB_RHILO	Q98cn7	rhizobium l
30	31	63.3	479	1	Y098_MYCPN	P75535	mycoplasma
31	31	63.3	1024	1	Y075_MYCGE	P47321	mycoplasma
32	30	61.2	78	1	RL31_RICCN	Q92jd0	rickettsia
33	30	61.2	78	1	RL31_RICPR	Q9ze47	rickettsia
34	30	61.2	197	1	OM26_HAEIN	Q57483	haemophilus
35	30	61.2	351	1	HI82_RHIME	Q92121	rhizobium m
36	30	61.2	356	1	RF1_BACSU	P45872	bacillus su
37	30	61.2	394	1	EFTU_BUCAI	O31297	buchnera ap
38	30	61.2	400	1	YF74_ARCFU	O28698	archaeoglob
39	30	61.2	419	1	P47K_PSECL	P31521	pseudomonas
40	30	61.2	463	1	YDI4_SCHPO	Q92342	schizosacch
41	30	61.2	464	1	SPN5_SCHPO	P48010	schizosacch
42	30	61.2	595	1	SYK_MOUSE	Q99mn1	mus musculu
43	30	61.2	656	1	V091_FOWPV	O72896	fowlpox vir
44	30	61.2	666	1	ZP2_RABIT	P48829	oryctolagus
45	30	61.2	681	1	THIC_YERPE	Q8zaq2	yersinia pe

ALIGNMENTS

RESULT 1
A4_URSMA
```
ID   A4_URSMA        STANDARD;      PRT;    57 AA.
AC   Q29149;
DT   01-NOV-1997 (Rel. 35, Created)
DT   01-NOV-1997 (Rel. 35, Last sequence update)
DT   30-MAY-2000 (Rel. 39, Last annotation update)
DE   Alzheimer's disease amyloid A4 protein homolog [Contains: Beta-amyloid
DE   protein (Beta-APP) (A-beta)] (Fragment).
GN   APP.
OS   Ursus maritimus (Polar bear) (Thalarctos maritimus).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC   Mammalia; Eutheria; Carnivora; Fissipedia; Ursidae; Ursus.
OX   NCBI_TaxID=29073;
RN   [1]
RP   SEQUENCE FROM N.A.
RC   TISSUE=Brain;
RX   MEDLINE=92017079; PubMed=1656157;
RA   Johnstone E.M., Chaney M.O., Norris F.H., Pascual R., Little S.P.;
RT   "Conservation of the sequence of the Alzheimer's disease amyloid
RT   peptide in dog, polar bear and five other mammals by cross-species
RT   polymerase chain reaction analysis.";
RL   Brain Res. Mol. Brain Res. 10:299-305(1991).
CC   -!- FUNCTION: FUNCTIONAL NEURONAL RECEPTOR WHICH COUPLES TO
```

```
CC        INTRACELLULAR SIGNALING PATHWAY THROUGH THE GTP-BINDING PROTEIN
CC        G(O) (BY SIMILARITY).
CC     -!- SUBCELLULAR LOCATION: Type I membrane protein.
CC     -!- SIMILARITY: BELONGS TO THE APP FAMILY.
CC     -----------------------------------------------------------------
CC     This SWISS-PROT entry is copyright. It is produced through a collaboration
CC     between the Swiss Institute of Bioinformatics and the EMBL outstation -
CC     the European Bioinformatics Institute. There are no restrictions on its
CC     use by non-profit institutions as long as its content is in no way
CC     modified and this statement is not removed. Usage by and for commercial
CC     entities requires a license agreement (See http://www.isb-sib.ch/announce/
CC     or send an email to license@isb-sib.ch).
CC     -----------------------------------------------------------------
DR     EMBL; X56128; CAA39593.1; -.
DR     PIR; B60045; B60045.
DR     HSSP; P05067; 1BA4.
DR     InterPro; IPR001868; A4_APP.
DR     InterPro; IPR001255; Beta-APP.
DR     Pfam; PF03494; Beta-APP; 1.
DR     PROSITE; PS00319; A4_EXTRA; PARTIAL.
DR     PROSITE; PS00320; A4_INTRA; PARTIAL.
KW     Glycoprotein; Amyloid; Neurone; Transmembrane.
FT     NON_TER        1      1
FT     CHAIN          6     48        BETA-AMYLOID PROTEIN (POTENTIAL).
FT     DOMAIN        <1     33        EXTRACELLULAR (POTENTIAL).
FT     TRANSMEM      34     57        POTENTIAL.
FT     NON_TER       57     57
SQ     SEQUENCE    57 AA;   6172 MW;   84209D88EBA82DFA CRC64;

   Query Match            100.0%;   Score 49;   DB 1;   Length 57;
   Best Local Similarity   100.0%;   Pred. No. 0.0019;
   Matches    10;   Conservative     0;   Mismatches     0;   Indels     0;   Gaps     0;

Qy         1 SEVKMDAEFR 10
             ||||||||||
Db         1 SEVKMDAEFR 10


RESULT 2
A4_CANFA
ID     A4_CANFA       STANDARD;       PRT;      58 AA.
AC     Q28280;
DT     01-NOV-1997 (Rel. 35, Created)
DT     01-NOV-1997 (Rel. 35, Last sequence update)
DT     30-MAY-2000 (Rel. 39, Last annotation update)
DE     Alzheimer's disease amyloid A4 protein homolog [Contains: Beta-amyloid
DE     protein (Beta-APP) (A-beta)] (Fragment).
GN     APP.
OS     Canis familiaris (Dog).
OC     Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC     Mammalia; Eutheria; Carnivora; Fissipedia; Canidae; Canis.
OX     NCBI_TaxID=9615;
RN     [1]
RP     SEQUENCE FROM N.A.
RC     TISSUE=Kidney;
RX     MEDLINE=92017079; PubMed=1656157;
RA     Johnstone E.M., Chaney M.O., Norris F.H., Pascual R., Little S.P.;
```

RT   "Conservation of the sequence of the Alzheimer's disease amyloid
RT   peptide in dog, polar bear and five other mammals by cross-species
RT   polymerase chain reaction analysis.";
RL   Brain Res. Mol. Brain Res. 10:299-305(1991).
CC   -!- FUNCTION: FUNCTIONAL NEURONAL RECEPTOR WHICH COUPLES TO
CC   INTRACELLULAR SIGNALING PATHWAY THROUGH THE GTP-BINDING PROTEIN
CC   G(O) (BY SIMILARITY).
CC   -!- SUBCELLULAR LOCATION: Type I membrane protein.
CC   -!- SIMILARITY: BELONGS TO THE APP FAMILY.
CC   --
CC   This SWISS-PROT entry is copyright. It is produced through a collaboration
CC   between the Swiss Institute of Bioinformatics and the EMBL outstation -
CC   the European Bioinformatics Institute. There are no restrictions on its
CC   use by non-profit institutions as long as its content is in no way
CC   modified and this statement is not removed. Usage by and for commercial
CC   entities requires a license agreement (See http://www.isb-sib.ch/announce/
CC   or send an email to license@isb-sib.ch).
CC   --
DR   EMBL; X56125; CAA39590.1; -.
DR   HSSP; P05067; 1BA4.
DR   InterPro; IPR001868; A4_APP.
DR   InterPro; IPR001255; Beta-APP.
DR   Pfam; PF03494; Beta-APP; 1.
DR   PROSITE; PS00319; A4_EXTRA; PARTIAL.
DR   PROSITE; PS00320; A4_INTRA; PARTIAL.
KW   Glycoprotein; Amyloid; Neurone; Transmembrane.
FT   NON_TER   1   1
FT   CHAIN   7   49   BETA-AMYLOID PROTEIN (POTENTIAL).
FT   DOMAIN   <1   34   EXTRACELLULAR (POTENTIAL).
FT   TRANSMEM   35   58   POTENTIAL.
FT   NON_TER   58   58
SQ   SEQUENCE   58 AA;   6285 MW;   8469D488A2E12DFA CRC64;

   Query Match   100.0%; Score 49; DB 1; Length 58;
   Best Local Similarity   100.0%; Pred. No. 0.0019;
   Matches   10; Conservative   0; Mismatches   0; Indels   0; Gaps   0;

Qy   1 SEVKMDAEFR 10
                |||||||||||
Db   2 SEVKMDAEFR 11

RESULT 3
A4_RABIT
ID   A4_RABIT   STANDARD;   PRT;   58 AA.
AC   Q28748;
DT   01-NOV-1997 (Rel. 35, Created)
DT   01-NOV-1997 (Rel. 35, Last sequence update)
DT   16-OCT-2001 (Rel. 40, Last annotation update)
DE   Alzheimer's disease amyloid A4 protein homolog [Contains: Beta-amyloid
DE   protein (Beta-APP) (A-beta)] (Fragment).
GN   APP.
OS   Oryctolagus cuniculus (Rabbit).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC   Mammalia; Eutheria; Lagomorpha; Leporidae; Oryctolagus.
OX   NCBI_TaxID=9986;
RN   [1]

RP   SEQUENCE FROM N.A.
RC   TISSUE=Brain;
RX   MEDLINE=92017079; PubMed=1656157;
RA   Johnstone E.M., Chaney M.O., Norris F.H., Pascual R., Little S.P.;
RT   "Conservation of the sequence of the Alzheimer's disease amyloid
RT   peptide in dog, polar bear and five other mammals by cross-species
RT   polymerase chain reaction analysis.";
RL   Brain Res. Mol. Brain Res. 10:299-305(1991).
CC   -!- FUNCTION: FUNCTIONAL NEURONAL RECEPTOR WHICH COUPLES TO
CC   INTRACELLULAR SIGNALING PATHWAY THROUGH THE GTP-BINDING PROTEIN
CC   G(O) (BY SIMILARITY).
CC   -!- SUBCELLULAR LOCATION: Type I membrane protein.
CC   -!- SIMILARITY: BELONGS TO THE APP FAMILY.
CC   --
CC   This SWISS-PROT entry is copyright. It is produced through a collaboration
CC   between the Swiss Institute of Bioinformatics and the EMBL outstation -
CC   the European Bioinformatics Institute. There are no restrictions on its
CC   use by non-profit institutions as long as its content is in no way
CC   modified and this statement is not removed. Usage by and for commercial
CC   entities requires a license agreement (See http://www.isb-sib.ch/announce/
CC   or send an email to license@isb-sib.ch).
CC   --
DR   EMBL; X56129; CAA39594.1; -.
DR   HSSP; P05067; 1BA4.
DR   InterPro; IPR001868; A4_APP.
DR   InterPro; IPR001255; Beta-APP.
DR   Pfam; PF03494; Beta-APP; 1.
DR   PROSITE; PS00319; A4_EXTRA; PARTIAL.
DR   PROSITE; PS00320; A4_INTRA; PARTIAL.
KW   Glycoprotein; Amyloid; Neurone; Transmembrane.
FT   NON_TER   1   1
FT   CHAIN   6   48   BETA-AMYLOID PROTEIN (POTENTIAL).
FT   DOMAIN   <1   33   EXTRACELLULAR (POTENTIAL).
FT   TRANSMEM   34   57   POTENTIAL.
FT   DOMAIN   58   >58   CYTOPLASMIC (POTENTIAL).
FT   NON_TER   58   58
SQ   SEQUENCE   58 AA;   6300 MW;   F434209D88EBA82D CRC64;

    Query Match   100.0%; Score 49; DB 1; Length 58;
    Best Local Similarity   100.0%; Pred. No. 0.0019;
    Matches   10; Conservative   0; Mismatches   0; Indels   0; Gaps   0;

Qy   1 SEVKMDAEFR 10
              ||||||||||
Db   1 SEVKMDAEFR 10

RESULT 4
A4_SHEEP
ID   A4_SHEEP   STANDARD;   PRT;   58 AA.
AC   Q28757;
DT   01-NOV-1997 (Rel. 35, Created)
DT   01-NOV-1997 (Rel. 35, Last sequence update)
DT   30-MAY-2000 (Rel. 39, Last annotation update)
DE   Alzheimer's disease amyloid A4 protein homolog [Contains: Beta-amyloid
DE   protein (Beta-APP) (A-beta)] (Fragment).
GN   APP.

```
OS    Ovis aries (Sheep).
OC    Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC    Mammalia; Eutheria; Cetartiodactyla; Ruminantia; Pecora; Bovoidea;
OC    Bovidae; Caprinae; Ovis.
OX    NCBI_TaxID=9940;
RN    [1]
RP    SEQUENCE FROM N.A.
RC    TISSUE=Heart;
RX    MEDLINE=92017079; PubMed=1656157;
RA    Johnstone E.M., Chaney M.O., Norris F.H., Pascual R., Little S.P.;
RT    "Conservation of the sequence of the Alzheimer's disease amyloid
RT    peptide in dog, polar bear and five other mammals by cross-species
RT    polymerase chain reaction analysis.";
RL    Brain Res. Mol. Brain Res. 10:299-305(1991).
CC    -!- FUNCTION: FUNCTIONAL NEURONAL RECEPTOR WHICH COUPLES TO
CC        INTRACELLULAR SIGNALING PATHWAY THROUGH THE GTP-BINDING PROTEIN
CC        G(O) (BY SIMILARITY).
CC    -!- SUBCELLULAR LOCATION: Type I membrane protein.
CC    -!- SIMILARITY: BELONGS TO THE APP FAMILY.
CC    ------------------------------------------------------------------------
CC    This SWISS-PROT entry is copyright. It is produced through a collaboration
CC    between  the Swiss Institute of Bioinformatics  and the  EMBL outstation -
CC    the European Bioinformatics Institute.  There are no  restrictions on  its
CC    use  by  non-profit  institutions as long  as its content  is  in  no  way
CC    modified and this statement is not removed.  Usage  by  and for commercial
CC    entities requires a license agreement (See http://www.isb-sib.ch/announce/
CC    or send an email to license@isb-sib.ch).
CC    ------------------------------------------------------------------------
DR    EMBL; X56130; CAA39595.1; -.
DR    HSSP; P05067; 1BA4.
DR    InterPro; IPR001868; A4_APP.
DR    InterPro; IPR001255; Beta-APP.
DR    Pfam; PF03494; Beta-APP; 1.
DR    PROSITE; PS00319; A4_EXTRA; PARTIAL.
DR    PROSITE; PS00320; A4_INTRA; PARTIAL.
KW    Glycoprotein; Amyloid; Neurone; Transmembrane.
FT    NON_TER        1       1
FT    CHAIN          6      48        BETA-AMYLOID PROTEIN (POTENTIAL).
FT    DOMAIN        <1      33        EXTRACELLULAR (POTENTIAL).
FT    TRANSMEM      34      57        POTENTIAL.
FT    DOMAIN        58     >58        CYTOPLASMIC (POTENTIAL).
FT    NON_TER       58      58
SQ    SEQUENCE    58 AA;   6300 MW;   F434209D88EBA82D CRC64;

   Query Match            100.0%;  Score 49;  DB 1;  Length 58;
   Best Local Similarity  100.0%;  Pred. No. 0.0019;
   Matches   10;  Conservative   0;  Mismatches   0;  Indels   0;  Gaps   0;

Qy          1 SEVKMDAEFR 10
              ||||||||||
Db          1 SEVKMDAEFR 10


RESULT 5
A4_BOVIN
ID    A4_BOVIN       STANDARD;      PRT;     59 AA.
AC    Q28053;
```

```
DT    01-NOV-1997 (Rel. 35, Created)
DT    01-NOV-1997 (Rel. 35, Last sequence update)
DT    30-MAY-2000 (Rel. 39, Last annotation update)
DE    Alzheimer's disease amyloid A4 protein homolog [Contains: Beta-amyloid
DE    protein (Beta-APP) (A-beta)] (Fragment).
GN    APP.
OS    Bos taurus (Bovine).
OC    Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC    Mammalia; Eutheria; Cetartiodactyla; Ruminantia; Pecora; Bovoidea;
OC    Bovidae; Bovinae; Bos.
OX    NCBI_TaxID=9913;
RN    [1]
RP    SEQUENCE FROM N.A.
RC    TISSUE=Brain;
RX    MEDLINE=92017079; PubMed=1656157;
RA    Johnstone E.M., Chaney M.O., Norris F.H., Pascual R., Little S.P.;
RT    "Conservation of the sequence of the Alzheimer's disease amyloid
RT    peptide in dog, polar bear and five other mammals by cross-species
RT    polymerase chain reaction analysis.";
RL    Brain Res. Mol. Brain Res. 10:299-305(1991).
CC    -!- FUNCTION: FUNCTIONAL NEURONAL RECEPTOR WHICH COUPLES TO
CC        INTRACELLULAR SIGNALING PATHWAY THROUGH THE GTP-BINDING PROTEIN
CC        G(O) (BY SIMILARITY).
CC    -!- SUBCELLULAR LOCATION: Type I membrane protein.
CC    -!- SIMILARITY: BELONGS TO THE APP FAMILY.
CC    --------------------------------------------------------------------------
CC    This SWISS-PROT entry is copyright. It is produced through a collaboration
CC    between  the Swiss Institute of Bioinformatics  and the  EMBL outstation -
CC    the European Bioinformatics Institute.  There are no  restrictions on  its
CC    use  by  non-profit  institutions as long  as its content  is  in  no  way
CC    modified and this statement is not removed.  Usage  by  and for commercial
CC    entities requires a license agreement (See http://www.isb-sib.ch/announce/
CC    or send an email to license@isb-sib.ch).
CC    --------------------------------------------------------------------------
DR    EMBL; X56124; CAA39589.1; -.
DR    EMBL; X56126; CAA39591.1; -.
DR    HSSP; P05067; 1BA4.
DR    InterPro; IPR001868; A4_APP.
DR    InterPro; IPR001255; Beta-APP.
DR    Pfam; PF03494; Beta-APP; 1.
DR    PROSITE; PS00319; A4_EXTRA; PARTIAL.
DR    PROSITE; PS00320; A4_INTRA; PARTIAL.
KW    Glycoprotein; Amyloid; Neurone; Transmembrane.
FT    NON_TER        1      1
FT    CHAIN          7     49       BETA-AMYLOID PROTEIN (POTENTIAL).
FT    DOMAIN        <1     34       EXTRACELLULAR (POTENTIAL).
FT    TRANSMEM      35     58       POTENTIAL.
FT    DOMAIN        59    >59       CYTOPLASMIC (POTENTIAL).
FT    NON_TER       59     59
SQ    SEQUENCE    59 AA;   6414 MW;   F43469D488A2E12D CRC64;

   Query Match                  100.0%;  Score 49;  DB 1;  Length 59;
   Best Local Similarity   100.0%;  Pred. No. 0.0019;
   Matches    10;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy            1 SEVKMDAEFR 10
                ||||||||||
```

RESULT 6
A4_SAISC
ID   A4_SAISC   STANDARD;   PRT;   751 AA.
AC   Q95241;
DT   15-DEC-1998 (Rel. 37, Created)
DT   15-DEC-1998 (Rel. 37, Last sequence update)
DT   15-SEP-2003 (Rel. 42, Last annotation update)
DE   Amyloid beta A4 protein precursor (APP) (Alzheimer's disease amyloid
DE   protein homolog) [Contains: Soluble APP-alpha (S-APP-alpha); Soluble
DE   APP-beta (S-APP-beta); C99; Beta-amyloid protein 42 (Beta-APP42);
DE   Beta-amyloid protein 40 (Beta-APP40); C83; P3(42); P3(40); Gamma-
DE   CTF(59) (Gamma-secretase C-terminal fragment 59); Gamma-CTF(57)
DE   (Gamma-secretase C-terminal fragment 57); Gamma-CTF(50) (Gamma-
DE   secretase C-terminal fragment 50); C31].
GN   APP.
OS   Saimiri sciureus (Common squirrel monkey).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC   Mammalia; Eutheria; Primates; Platyrrhini; Cebidae; Cebinae; Saimiri.
OX   NCBI_TaxID=9521;
RN   [1]
RP   SEQUENCE FROM N.A.
RC   TISSUE=Kidney, and Liver;
RX   MEDLINE=96108492; PubMed=8532114;
RA   Levy E., Amorim A., Frangione B., Walker L.C.;
RT   "Beta-amyloid precursor protein gene in squirrel monkeys with
RT   cerebral amyloid angiopathy.";
RL   Neurobiol. Aging 16:805-808(1995).
CC   -!- FUNCTION: Functions as a cell surface receptor and performs
CC   physiological functions on the surface of neurons relevant to
CC   neurite growth, neuronal adhesion and axonogenesis. Involved in
CC   cell mobility and transcription regulation through protein-protein
CC   interactions (By similarity). Can promote transcription activation
CC   through binding to APBB1/Tip60 and inhibit Notch signaling through
CC   interaction with Numb (By similarity). Couples to apoptosis-
CC   inducing pathways such as those mediated by G(O) and JIP (By
CC   similarity). Inhibits G(O) alpha ATPase activity (By similarity).
CC   Acts as a kinesin I membrane receptor, mediating the axonal
CC   transport of beta-secretase and presenilin 1 (By similarity). May
CC   be involved in copper homeostasis/oxidative stress through copper
CC   ion reduction. In vitro, copper-metallated APP induces neuronal
CC   death directly or is potentiated through Cu(II)-mediated low-
CC   density lipoprotein oxidation (By similarity). Can regulate
CC   neurite outgrowth through binding to components of the
CC   extracellular matrix such as heparin and collagen I and IV (By
CC   similarity). The splice isoforms that contain the BPTI domain
CC   possess protease inhibitor activity (By similarity).
CC   -!- FUNCTION: Beta-amyloid peptides are lipophilic metal chelators
CC   with metal-reducing activity. Bind transient metals such as
CC   copper, zinc and iron (By similarity).
CC   -!- FUNCTION: The gamma-CTF peptides as well as the caspase-cleaved
CC   peptides, including C31, are potent enhancers of neuronal
CC   apoptosis (By similarity).
CC   -!- SUBUNIT: Binds, via its C-terminal, to the PID domain of several
CC   cytoplasmic proteins, including APBB family members, the APBA

CC   family, MAPK8IP1, and SHC1, Numb and Dab1 (By similarity). Binding
CC   to Dab1 inhibits its serine phosphorylation (By similarity). Also
CC   interacts with GPCR-like protein BPP, FPRL1, APPBP1, IB1, KNS2
CC   (via its TPR domains) (By similarity), APPBP2 (via BaSS) and DDB1.
CC   In vitro, it binds MAPT via the MT-binding domains (By
CC   similarity). Associates with microtubules in the presence of ATP
CC   and in a kinesin-dependent manner (By similarity).
CC   -!- SUBCELLULAR LOCATION: Type I membrane protein. Cell surface
CC   protein that rapidly becomes internalized via clatherin-coated
CC   pits. During maturation, the immature APP (N-glycosylated in the
CC   endoplasmic reticulum) moves to the Golgi complex where complete
CC   maturation occurs (O-glycosylated and sulfated). After alpha-
CC   secretase cleavage, soluble APP is released into the extracellular
CC   space and the C-terminal is internalized to endosomes and
CC   lysosomes. Some APP accumulates in secretory transport vesicles
CC   leaving the late Golgi compartment and returns to the cell
CC   surface. GammaCTF(59) peptide is located to both the cytoplasm and
CC   nuclei of neurons (By similarity).
CC   -!- ALTERNATIVE PRODUCTS:
CC   Event=Alternative splicing; Named isoforms=2;
CC   ᴸ   Comment=Additional isoforms seem to exist;
CC   Name=APP770;
CC   IsoId=Q95241-1; Sequence=Displayed;
CC   Name=APP695;
CC   IsoId=Q95241-2; Sequence=Not described;
CC   -!- DOMAIN: The basolateral sorting signal (BaSS) is required for
CC   sorting of membrane proteins to the basolateral surface of
CC   epithelial cells (By similarity).
CC   -!- DOMAIN: The NPXY sequence motif found in many tyrosine-
CC   phosphorylated proteins is required for the specific binding of
CC   the PID domain. However additional amino acids either N- or C-
CC   terminal to the NPXY motif are often required for complete
CC   interaction. The PID domain-containing proteins which bind APP
CC   require the YENPTY motif for full interaction. These interactions
CC   are independent of phosphorylation on the terminal tyrosine
CC   residue. The NPXY site is also involved in clatherin-mediated
CC   endocytosis (By similarity).
CC   -!- PTM: Proteolytically processed under normal cellular conditions.
CC   Cleavage by alpha-secretase or alternatively by beta-secretase
CC   leads to generation and extracellular release of soluble APP
CC   peptides, S-APP-alpha and S-APP-beta, respectively, and the
CC   retention of corresponding membrane-anchored C-terminal fragments,
CC   C83 and C99. Subsequent processing of C83 by gamma-secretase
CC   yields P3 peptides. This is the major secretory pathway and is
CC   nonamyloidogenic. Alternatively, presenilin/nicastrin-mediated
CC   gamma-secretase processing of C99 releases the amyloid beta
CC   proteins, amyloid-beta 40 (Abeta40) and amyloid-beta 42 (Abeta42),
CC   major components of amyloid plaques, and the cytotoxic C-terminal
CC   fragments, gammaCTF(50), gammaCTF(57) and gammaCTF(59) (By
CC   similarity).
CC   -!- PTM: Proteolytically cleaved by caspases during neuronal apoptosis
CC   (By similarity). Cleavage at Asp-720 by either caspase-3, -8 or -9
CC   results in the production of the neurotoxic C31 peptide and the
CC   increased production of beta-amyloid peptides (By similarity).
CC   -!- PTM: N- and O-linked glycosylated (By similarity).
CC   -!- PTM: Phosphorylation in the C-terminal on tyrosine, threonine and
CC   serine residues is neuron-specific. Phosphorylation can affect APP

```
CC          processing, neuronal differentiation and interaction with other
CC          proteins (By similarity).
CC       -!- MISCELLANEOUS: Chelation of metal ions, notably copper, iron and
CC          zinc, can induce histidine-bridging between beta-amyloid molecules
CC          resulting in beta-amyloid-metal aggregates (By similarity).
CC          Extracellular zinc-binding increases binding of heparin to APP and
CC          inhibits collagen-binding (By similarity).
CC       -!- SIMILARITY: BELONGS TO THE APP FAMILY.
CC       -!- SIMILARITY: Contains 1 BPTI/Kunitz inhibitor domain.
CC       -----------------------------------------------------------------------
CC       This SWISS-PROT entry is copyright. It is produced through a collaboration
CC       between  the Swiss Institute of Bioinformatics  and the  EMBL outstation -
CC       the European Bioinformatics Institute.  There are no  restrictions on  its
CC       use  by  non-profit  institutions as long  as its content  is  in  no  way
CC       modified and this statement is not removed.  Usage  by  and for commercial
CC       entities requires a license agreement (See http://www.isb-sib.ch/announce/
CC       or send an email to license@isb-sib.ch).
CC       -----------------------------------------------------------------------
DR       EMBL; S81024; AAD14347.1; -.
DR       HSSP; P05067; 1AAP.
DR       InterPro; IPR001868; A4_APP.
DR       InterPro; IPR001255; Beta-APP.
DR       InterPro; IPR002223; Kunitz_BPTI.
DR       Pfam; PF02177; A4_EXTRA; 1.
DR       Pfam; PF03494; Beta-APP; 1.
DR       Pfam; PF00014; Kunitz_BPTI; 1.
DR       PRINTS; PR00203; AMYLOIDA4.
DR       PRINTS; PR00759; BASICPTASE.
DR       ProDom; PD000222; Kunitz_BPTI; 1.
DR       SMART; SM00006; A4_EXTRA; 1.
DR       SMART; SM00131; KU; 1.
DR       PROSITE; PS00319; A4_EXTRA; 1.
DR       PROSITE; PS00320; A4_INTRA; 1.
DR       PROSITE; PS00280; BPTI_KUNITZ_1; 1.
DR       PROSITE; PS50279; BPTI_KUNITZ_2; 1.
KW       Apoptosis; Endocytosis; Cell adhesion; Serine protease inhibitor;
KW       Coated pits; Neurone; Heparin-binding; Metal-binding; Copper; Iron;
KW       Zinc; Signal; Transmembrane; Glycoprotein; Phosphorylation;
KW       Proteoglycan; Amyloid; Alternative splicing.
FT       SIGNAL        1      17       BY SIMILARITY.
FT       CHAIN        18     751       A4 PROTEIN.
FT       CHAIN        18     668       SOLUBLE APP-ALPHA (POTENTIAL).
FT       CHAIN        18     652       SOLUBLE APP-BETA (POTENTIAL).
FT       CHAIN       653     751       C99 (POTENTIAL).
FT       CHAIN       653     694       BETA-AMYLOID PROTEIN 42 (POTENTIAL).
FT       CHAIN       653     692       BETA-AMYLOID PROTEIN 40 (POTENTIAL).
FT       CHAIN       669     751       C83 (POTENTIAL).
FT       CHAIN       669     694       P3(42) (POTENTIAL).
FT       CHAIN       669     692       P3(40) (POTENTIAL).
FT       CHAIN       693     751       GAMMA-CTF(59) (POTENTIAL).
FT       CHAIN       695     751       GAMMA-CTF(57) (POTENTIAL).
FT       CHAIN       702     751       GAMMA-CTF(50) (POTENTIAL).
FT       CHAIN       721     751       C31 (POTENTIAL).
FT       DOMAIN       18     680       EXTRACELLULAR (POTENTIAL).
FT       TRANSMEM    681     704       POTENTIAL.
FT       DOMAIN      705     751       CYTOPLASMIC (POTENTIAL).
FT       DOMAIN       96     110       HEPARIN-BINDING (BY SIMILARITY).
```

```
FT   DOMAIN      181    188    ZINC-BINDING (BY SIMILARITY).
FT   DOMAIN      291    341    BPTI/KUNITZ INHIBITOR.
FT   DOMAIN      316    344    HEPARIN-BINDING (BY SIMILARITY).
FT   DOMAIN      363    428    HEPARIN-BINDING (BY SIMILARITY).
FT   DOMAIN      504    521    COLLAGEN-BINDING (BY SIMILARITY).
FT   DOMAIN      713    732    INTERACTION WITH G(O)-ALPHA
FT                             (BY SIMILARITY).
FT   DOMAIN      230    260    ASP/GLU-RICH (ACIDIC).
FT   DOMAIN      274    280    POLY-THR.
FT   SITE        144    144    REQUIRED FOR COPPER(II) REDUCTION
FT                             (BY SIMILARITY).
FT   ACT_SITE    301    302    REACTIVE BOND.
FT   SITE        652    653    CLEAVAGE (BY BETA-SECRETASE)
FT                             (BY SIMILARITY).
FT   SITE        653    654    CLEAVAGE (BY CASPASE-6) (BY SIMILARITY).
FT   SITE        668    669    CLEAVAGE (BY ALPHA-SECRETASE)
FT                             (BY SIMILARITY).
FT   SITE        685    685    INVOLVED IN FREE RADICAL PROPAGATION
FT                             (BY SIMILARITY).
FT   SITE        687    687    INVOLVED IN OXIDATIVE REACTIONS
FT                             (BY SIMILARITY).
FT   SITE        692    693    CLEAVAGE (BY GAMMA-SECRETASE; SITE 1)
FT                             (BY SIMILARITY).
FT   SITE        694    695    CLEAVAGE (BY GAMMA-SECRETASE; SITE 2)
FT                             (BY SIMILARITY).
FT   SITE        701    702    CLEAVAGE (BY GAMMA-SECRETASE; SITE 3)
FT                             (BY SIMILARITY).
FT   SITE        705    715    BASOLATERAL SORTING SIGNAL
FT                             (BY SIMILARITY).
FT   SITE        720    721    CLEAVAGE (BY CASPASES-3,-6,-8 OR -9)
FT                             (BY SIMILARITY).
FT   SITE        738    741    ENDOCYTOSIS SIGNAL.
FT   SITE        740    743    NPXY MOTIF.
FT   METAL       137    137    COPPER (BY SIMILARITY).
```

```
Query Match            100.0%;  Score 49;  DB 1;  Length 751;
Best Local Similarity  100.0%;  Pred. No. 0.024;
Matches    10;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy       1 SEVKMDAEFR 10
           ||||||||||
Db     648 SEVKMDAEFR 657
```

RESULT 7
A4_CAVPO
```
ID   A4_CAVPO       STANDARD;      PRT;   770 AA.
AC   Q60495; Q60496;
DT   15-SEP-2003 (Rel. 42, Created)
DT   15-SEP-2003 (Rel. 42, Last sequence update)
DT   15-SEP-2003 (Rel. 42, Last annotation update)
DE   Amyloid beta A4 protein precursor (APP) (ABPP) (Alzheimer's disease
DE   amyloid protein homolog) [Contains: Soluble APP-alpha (S-APP-alpha);
DE   Soluble APP-beta (S-APP-beta); CTF-alpha; CTF-beta; Beta-amyloid
DE   protein 42 (Beta-APP42); Beta-amyloid protein 40 (Beta-APP40); P3(42);
DE   P3(40); CTF(59) (Gamma-secretase C-terminal fragment 59); Gamma-
DE   CTF(57) (Gamma-secretase C-terminal fragment 57); C31].
```

```
GN   APP.
OS   Cavia porcellus (Guinea pig).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC   Mammalia; Eutheria; Rodentia; Hystricognathi; Caviidae; Cavia.
OX   NCBI_TaxID=10141;
RN   [1]
RP   SEQUENCE FROM N.A., AND ALTERNATIVE SPLICING.
RC   TISSUE=Brain, and Liver;
RX   MEDLINE=97236426; PubMed=9116031;
RA   Beck M., Mueller D., Bigl V.;
RT   "Amyloid precursor protein in Guinea pigs - complete cDNA sequence and
RT   alternative splicing.";
RL   Biochim. Biophys. Acta 1351:17-21(1997).
RN   [2]
RP   INTERACTION OF BETA-APP40 WITH APOE.
RX   MEDLINE=98007700; PubMed=9349544;
RA   Martel C.L., Mackic J.B., Matsubara E., Governale S., Miguel C.,
RA   Miao W., McComb J.G., Frangione B., Ghiso J., Zlokovic B.V.;
RT   "Isoform-specific effects of apolipoproteins E2, E3, and E4 on
RT   cerebral capillary sequestration and blood-brain barrier transport of
RT   circulating Alzheimer's amyloid beta.";
RL   J. Neurochem. 69:1995-2004(1997).
RN   [3]
RP   PROCESSING.
RX   MEDLINE=20084499; PubMed=10619481;
RA   Beck M., Brueckner M.K., Holzer M., Kaap S., Pannicke T., Arendt T.,
RA   Bigl V.;
RT   "Guinea-pig primary cell cultures provide a model to study expression
RT   and amyloidogenic processing of endogenous amyloid precursor
RT   protein.";
RL   Neuroscience 95:243-254(2000).
RN   [4]
RP   GAMMA-SECRETASE PROCESSING.
RX   MEDLINE=20576391; PubMed=11035007;
RA   Pinnix I., Musunuru U., Tun H., Sridharan A., Golde T., Eckman C.,
RA   Ziani-Cherif C., Onstead L., Sambamurti K.;
RT   "A novel gamma -secretase assay based on detection of the putative
RT   C-terminal fragment-gamma of amyloid beta protein precursor.";
RL   J. Biol. Chem. 276:481-487(2001).
CC   -!- FUNCTION: Functions as a cell surface receptor and performs
CC       physiological functions on the surface of neurons relevant to
CC       neurite growth, neuronal adhesion and axonogenesis. Involved in
CC       cell mobility and transcription regulation through protein-protein
CC       interactions (By similarity). Can promote transcription activation
CC       through binding to APBB1/Tip60 and inhibit Notch signaling through
CC       interaction with Numb (By similarity). Couples to apoptosis-
CC       inducing pathways such as those mediated by G(O) and JIP (By
CC       similarity). Inhibits G(O) alpha ATPase activity (By similarity).
CC       Acts as a kinesin I membrane receptor, mediating the axonal
CC       transport of beta-secretase and presenilin 1 (By similarity). May
CC       be involved in copper homeostasis/oxidative stress through copper
CC       ion reduction (By similarity). In vitro, copper-metallated APP
CC       induces neuronal death directly or is potentiated through Cu(II)-
CC       mediated low-density lipoprotein oxidation (By similarity). Can
CC       regulate neurite outgrowth through binding to components of the
CC       extracellular matrix such as heparin and collagen I and IV (By
CC       similarity). The splice isoforms that contain the BPTI domain
```

```
CC            possess protease inhibitor activity (By similarity).
CC     -!- FUNCTION: Beta-amyloid peptides are lipophilic metal chelators
CC            with metal-reducing activity. Bind transient metals such as
CC            copper, zinc and iron. Beta-amyloid peptides bind to lipoproteins
CC            and apolipoproteins E and J in the CSF and to HDL particles in
CC            plasma, inhibiting metal-catalyzed oxidation of lipoproteins.
CC     -!- FUNCTION: Appicans elicit adhesion of neural cells to the
CC            extracellular matrix and may regulate neurite outgrowth in the
CC            brain (By similarity).
CC     -!- FUNCTION: The gamma-CTF peptides as well as the caspase-cleaved
CC            peptides, including C31, are potent enhancers of neuronal
CC            apoptosis (By similarity).
CC     -!- SUBUNIT: Binds, via its C-terminal, to the PID domain of several
CC            cytoplasmic proteins, including APBB family members, the APBA
CC            family, MAPK8IP1, SHC1 and Numb and Dab1 (By similarity). Also
CC            interacts with GPCR-like protein BPP, FPRL1, APPBP1, IB1, KNS2
CC            (via its TPR domains), APPBP2 (via BaSS) and DDB1 (By similarity).
CC            Associates with microtubules in the presence of ATP and in a
CC            kinesin-dependent manner (By similarity). Soluble Abeta40 binds
CC            all three isoforms of APOE, in vitro and in vivo. When lipidated,
CC            ApoE3 appears to be the preferred amyloid binding isoform, while
CC            the apoE4 isoform-beta-APP40 complex is capable of being
CC            transported across the blood-brain barrier.
CC     -!- SUBCELLULAR LOCATION: Type I membrane protein. Cell surface
CC            protein that rapidly becomes internalized via clathrin-coated pits
CC            (By similarity). During maturation, the immature APP (N-
CC            glycosylated in the endoplasmic reticulum) moves to the Golgi
CC            complex where complete maturation occurs (O-glycosylated and
CC            sulfated) (By similarity). After alpha-secretase cleavage, soluble
CC            APP is released into the extracellular space and the C-terminal is
CC            internalized to endosomes and lysosomes (By similarity). Some APP
CC            accumulates in secretory transport vesicles leaving the late Golgi
CC            compartment and returns to the cell surface (By similarity). APP
CC            sorts to the basolateral surface in epithelial cells (By
CC            similatity).
CC     -!- ALTERNATIVE PRODUCTS:
CC            Event=Alternative splicing; Named isoforms=2;
CC              Comment=Additional isoforms, missing exons 7,8 and 15, seem to
CC              exist. The L-isoforms, missing exon 15, are referred to as
CC              appicans;
CC            Name=APP770;
CC              IsoId=Q60495-1; Sequence=Displayed;
CC            Name=APP695;
CC              IsoId=Q60495-2; Sequence=VSP_007221, VSP_007222;
CC     -!- TISSUE SPECIFICITY: Isoform APP695 is the major isoform found in
CC            brain. The longer isoforms containing the BPTI domain are
CC            predominantly expressed in peripheral organs such as muscle and
CC            liver.
CC     -!- INDUCTION: Increased levels during neuronal differentiation.
CC     -!- DOMAIN: The basolateral sorting signal (BaSS) is required for
CC            sorting of membrane proteins to the basolateral surface of
CC            epithelial cells.
CC     -!- DOMAIN: The NPXY sequence motif found in many tyrosine-
CC            phosphorylated proteins is required for the specific binding of
CC            the PID domain. However additional amino acids either N- or C-
CC            terminal to the NPXY motif are often required for complete
CC            interaction. The PID domain-containing proteins which bind APP
```

```
CC        require the YENPTY motif for full interaction. These interactions
CC        are independent of phosphorylation on the terminal tyrosine
CC        residue (By similarity). The NPXY site is also involved in
CC        clatherin-mediated endocytosis.
CC     -!- PTM: Proteolytically processed under normal cellular conditions.
CC        Cleavage by alpha-secretase or alternatively by beta-secretase
CC        leads to generation and extracellular release of soluble APP
CC        peptides, S-APP-alpha and S-APP-beta, respectively, and the
CC        retention of corresponding membrane-anchored C-terminal fragments,
CC        CTF-alpha and CTF-beta. Subsequent processing of CTF-alpha by
CC        gamma-secretase yields P3 peptides. This is the major secretory
CC        pathway and is nonamyloidogenic. Alternatively,
CC        presenilin/nicastrin-mediated gamma-secretase processing of CTF-
CC        beta releases the amyloid beta proteins, amyloid-beta 40 (Abeta40)
CC        and amyloid-beta 42 (Abeta42), major components of amyloid
CC        plaques, and the corresponding cytotoxic C-terminal fragments
CC        (CTFs).
CC     -!- PTM: Proteolytically cleaved by caspase-3 during neuronal
CC        apoptosis (By similarity).
CC     -!- PTM: N- and O-linked glycosylated. O-linkage of chondroitin
CC        sulfate to the L-APP isoforms produces the APP proteoglycan core
CC        proteins, the appicans (By similarity).
CC     -!- PTM: Phosphorylation in the C-terminal on tyrosine, threonine and
CC        serine residues is neuron-specific (By similarity).
CC        Phosphorylation can affect APP processing, neuronal
CC        differentiation and interaction with other proteins.
CC     -!- PTM: Extracellular binding and reduction of copper, results in a
CC        corresponding oxidation of Cys-144 and Cys-158, and the formation
CC        of a disulfide bond (By similarity).
CC     -!- MISCELLANEOUS: Chelation of metal ions, notably copper, iron and
CC        zinc, can induce histidine-bridging between beta-amyloid molecules
CC        resulting in beta-amyloid-metal aggregates.
CC     -!- SIMILARITY: BELONGS TO THE APP FAMILY.
CC     -!- SIMILARITY: Contains 1 BPTI/Kunitz inhibitor domain.
CC     ----------------------------------------------------------------------
CC     This SWISS-PROT entry is copyright. It is produced through a collaboration
CC     between  the Swiss Institute of Bioinformatics  and the  EMBL outstation -
CC     the European Bioinformatics Institute.  There are no  restrictions on  its
CC     use  by  non-profit  institutions as long  as its content  is  in  no  way
CC     modified and this statement is not removed.  Usage  by  and for commercial
CC     entities requires a license agreement (See http://www.isb-sib.ch/announce/
CC     or send an email to license@isb-sib.ch).
CC     ----------------------------------------------------------------------
DR     EMBL; X97631; CAA66230.1; -.
DR     EMBL; X99198; CAA67589.1; -.
DR     HSSP; P05067; 1BA4.
DR     InterPro; IPR008155; A4_APP.
DR     InterPro; IPR008154; A4_extra.
DR     InterPro; IPR001255; Beta-APP.
DR     Pfam; PF00014; Kunitz_BPTI; 1.
DR     PRINTS; PR00203; AMYLOIDA4.
DR     ProDom; PD000222; Kunitz_BPTI; 1.
DR     SMART; SM00006; A4_EXTRA; 1.
DR     SMART; SM00131; KU; 1.
DR     PROSITE; PS00319; A4_EXTRA; 1.
DR     PROSITE; PS00320; A4_INTRA; 1.
DR     PROSITE; PS00280; BPTI_KUNITZ_1; 1.
```

```
DR   PROSITE; PS50279; BPTI_KUNITZ_2; 1.
KW   Apoptosis; Endocytosis; Cell adhesion; Serine protease inhibitor;
KW   Coated pits; Neurone; Heparin-binding; Metal-binding; Copper; Iron;
KW   Zinc; Signal; Transmembrane; Glycoprotein; Phosphorylation;
KW   Proteoglycan; Alternative splicing; Amyloid.
FT   SIGNAL        1     17       BY SIMILARITY.
FT   CHAIN        18    770       AMYLOID BETA A4 PROTEIN.
FT   CHAIN        18    687       SOLUBLE APP-ALPHA (BY SIMILARITY).
FT   CHAIN        18    671       SOLUBLE APP-BETA (BY SIMILARITY).
FT   CHAIN       672    770       CTF-ALPHA (BY SIMILARITY).
FT   CHAIN       672    713       BETA-AMYLOID PROTEIN 42 (BY SIMILARITY).
FT   CHAIN       672    711       BETA-AMYLOID PROTEIN 40 (BY SIMILARITY).
FT   CHAIN       688    770       CTF-BETA (BY SIMILARITY).
FT   CHAIN       688    713       P3(42) (BY SIMILARITY).
FT   CHAIN       688    711       P3(40) (BY SIMILARITY).
FT   CHAIN       712    770       GAMMA-CTF(59) (BY SIMILARITY).
FT   CHAIN       714    770       GAMMA-CTF(57) (BY SIMILARITY).
FT   CHAIN       740    770       C31 (BY SIMILARITY).

     Query Match              100.0%;  Score 49;  DB 1;  Length 770;
     Best Local Similarity    100.0%;  Pred. No. 0.025;
     Matches   10;  Conservative   0;  Mismatches   0;  Indels   0;  Gaps   0;

Qy         1 SEVKMDAEFR 10
             ||||||||||
Db       667 SEVKMDAEFR 676


RESULT 8
A4_HUMAN
ID   A4_HUMAN      STANDARD;      PRT;   770 AA.
AC   P05067; P09000; P78438; Q13764; Q13778; Q13793; Q16011; Q9BT38;
AC   Q9UCB6; Q9UQ58;
DT   13-AUG-1987 (Rel. 05, Created)
DT   01-NOV-1991 (Rel. 20, Last sequence update)
DT   15-SEP-2003 (Rel. 42, Last annotation update)
DE   Amyloid beta A4 protein precursor (APP) (ABPP) (Alzheimer's disease
DE   amyloid protein) (Cerebral vascular amyloid peptide) (CVAP) (Protease
DE   nexin-II) (PN-II) (APPI) (PreA4) [Contains: Soluble APP-alpha (S-APP-
DE   alpha); Soluble APP-beta (S-APP-beta); C99; Beta-amyloid protein 42
DE   (Beta-APP42); Beta-amyloid protein 40 (Beta-APP40); C83; P3(42);
DE   P3(40); Gamma-CTF(59) (Gamma-secretase C-terminal fragment 59)
DE   (Amyloid intracellular domain 59) (AID(59)); Gamma-CTF(57) (Gamma-
DE   secretase C-terminal fragment 57) (Amyloid intracellular domain 57)
DE   (AID(57)); Gamma-CTF(50) (Gamma-secretase C-terminal fragment 50)
DE   (Amyloid intracellular domain 50) (AID(50)); C31].
GN   APP OR A4 OR AD1.
OS   Homo sapiens (Human).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC   Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
OX   NCBI_TaxID=9606;
RN   [1]
RP   SEQUENCE FROM N.A. (ISOFORM APP695).
RC   TISSUE=Brain;
RX   MEDLINE=87144572; PubMed=2881207;
RA   Kang J., Lemaire H.-G., Unterbeck A., Salbaum J.M., Masters C.L.,
RA   Grzeschik K.-H., Multhaup G., Beyreuther K., Mueller-Hill B.;
```

RT   "The precursor of Alzheimer's disease amyloid A4 protein resembles a
RT   cell-surface receptor.";
RL   Nature 325:733-736(1987).
RN   [2]
RP   SEQUENCE FROM N.A. (ISOFORM APP751).
RC   TISSUE=Brain;
RX   MEDLINE=88122639; PubMed=2893289;
RA   Ponte P., Gonzalez-Dewhitt P., Schilling J., Miller J., Hsu D.,
RA   Greenberg B., Davis K., Wallace W., Lieberburg I., Fuller F.,
RA   Cordell B.;
RT   "A new A4 amyloid mRNA contains a domain homologous to serine
RT   proteinase inhibitors.";
RL   Nature 331:525-527(1988).
RN   [3]
RP   SEQUENCE FROM N.A. (ISOFORM APP695).
RX   MEDLINE=89128427; PubMed=2783775;
RA   Lemaire H.-G., Salbaum J.M., Multhaup G., Kang J., Bayney R.M.,
RA   Unterbeck A., Beyreuther K., Mueller-Hill B.;
RT   "The PreA4(695) precursor protein of Alzheimer's disease A4 amyloid
RT   is encoded by 16 exons.";
RL   Nucleic Acids Res. 17:517-522(1989).
RN   [4]
RP   SEQUENCE FROM N.A. (ISOFORM APP770).
RX   MEDLINE=90236318; PubMed=2110105;
RA   Yoshikai S.-I., Sasaki H., Doh-Ura K., Furuya H., Sakaki Y.;
RT   "Genomic organization of the human amyloid beta-protein precursor
RT   gene.";
RL   Gene 87:257-263(1990).
RN   [5]
RP   ERRATUM, AND REVISIONS.
RA   Yoshikai S.-I., Sasaki H., Doh-ura K., Furuya H., Sakaki Y.;
RL   Gene 102:291-292(1991).
RN   [6]
RP   SEQUENCE FROM N.A. (ISOFORM L-APP733).
RC   TISSUE=Leukocyte;
RX   MEDLINE=92268136; PubMed=1587857;
RA   Koenig G., Moenning U., Czech C., Prior R., Banati R.,
RA   Schreiter-Gasser U., Bauer J., Masters C.L., Beyreuther K.;
RT   "Identification and differential expression of a novel alternative
RT   splice isoform of the beta A4 amyloid precursor protein (APP) mRNA in
RT   leukocytes and brain microglial cells.";
RL   J. Biol. Chem. 267:10804-10809(1992).
RN   [7]
RP   SEQUENCE FROM N.A. (ISOFORM APP770).
RX   MEDLINE=97263807; PubMed=9108164;
RA   Hattori M., Tsukahara F., Furuhata Y., Tanahashi H., Hirose M.,
RA   Saito M., Tsukuni S., Sakaki Y.;
RT   "A novel method for making nested deletions and its application for
RT   sequencing of a 300 kb region of human APP locus.";
RL   Nucleic Acids Res. 25:1802-1808(1997).
RN   [8]
RP   SEQUENCE FROM N.A. (ISOFORM APP305).
RC   TISSUE=Pancreas;
RX   MEDLINE=22388257; PubMed=12477932;
RA   Strausberg R.L., Feingold E.A., Grouse L.H., Derge J.G.,
RA   Klausner R.D., Collins F.S., Wagner L., Shenmen C.M., Schuler G.D.,
RA   Altschul S.F., Zeeberg B., Buetow K.H., Schaefer C.F., Bhat N.K.,

RA   Hopkins R.F., Jordan H., Moore T., Max S.I., Wang J., Hsieh F.,
RA   Diatchenko L., Marusina K., Farmer A.A., Rubin G.M., Hong L.,
RA   Stapleton M., Soares M.B., Bonaldo M.F., Casavant T.L., Scheetz T.E.,
RA   Brownstein M.J., Usdin T.B., Toshiyuki S., Carninci P., Prange C.,
RA   Raha S.S., Loquellano N.A., Peters G.J., Abramson R.D., Mullahy S.J.,
RA   Bosak S.A., McEwan P.J., McKernan K.J., Malek J.A., Gunaratne P.H.,
RA   Richards S., Worley K.C., Hale S., Garcia A.M., Gay L.J., Hulyk S.W.,
RA   Villalon D.K., Muzny D.M., Sodergren E.J., Lu X., Gibbs R.A.,
RA   Fahey J., Helton E., Ketteman M., Madan A., Rodrigues S., Sanchez A.,
RA   Whiting M., Madan A., Young A.C., Shevchenko Y., Bouffard G.G.,
RA   Blakesley R.W., Touchman J.W., Green E.D., Dickson M.C.,
RA   Rodriguez A.C., Grimwood J., Schmutz J., Myers R.M.,
RA   Butterfield Y.S.N., Krzywinski M.I., Skalska U., Smailus D.E.,
RA   Schnerch A., Schein J.E., Jones S.J.M., Marra M.A.;
RT   "Generation and initial analysis of more than 15,000 full-length
RT   human and mouse cDNA sequences.";
RL   Proc. Natl. Acad. Sci. U.S.A. 99:16899-16903(2002).
RN   [9]
RP   SEQUENCE OF 1-10 FROM N.A.
RC   TISSUE=Liver;
RX   MEDLINE=89016647; PubMed=3140222;
RA   Schon E.A., Mita S., Sadlock J., Herbert J.;
RT   "A cDNA specifying the human amyloid beta precursor protein (ABPP)
RT   encodes a 95-kDa polypeptide.";
RL   Nucleic Acids Res. 16:9351-9351(1988).
RN   [10]
RP   ERRATUM, AND REVISIONS.
RA   Mita S., Sadlock J., Herbert J., Schon E.A.;
RL   Nucleic Acids Res. 16:11402-11402(1988).
RN   [11]
RP   SEQUENCE OF 1-75 FROM N.A.
RX   MEDLINE=89165870; PubMed=2538123;
RA   La Fauci G., Lahiri D.K., Salton S.R., Robakis N.K.;
RT   "Characterization of the 5'-end region and the first two exons of the
RT   beta-protein precursor gene.";
RL   Biochem. Biophys. Res. Commun. 159:297-304(1989).
RN   [12]
RP   SEQUENCE OF 18-50.
RC   TISSUE=Fibroblast;
RX   MEDLINE=87250462; PubMed=3597385;
RA   van Nostrand W.E., Cunningham D.D.;
RT   "Purification of protease nexin II from human fibroblasts.";
RL   J. Biol. Chem. 262:8508-8514(1987).
RN   [13]
RP   PARTIAL SEQUENCE FROM N.A. (ISOFORM APP751).
RC   TISSUE=Brain;
RX   MEDLINE=89346754; PubMed=2569763;
RA   de Sauvage F., Octave J.N.;
RT   "A novel mRNA of the A4 amyloid precursor gene coding for a possibly
RT   secreted protein.";
RL   Science 245:651-653(1989).
RN   [14]
RP   PARTIAL SEQUENCE FROM N.A. (ISOFORM APP695).
RC   TISSUE=Brain;
RX   MEDLINE=87231971; PubMed=3035574;
RA   Robakis N.K., Ramakrishna N., Wolfe G., Wisniewski H.M.;
RT   "Molecular cloning and characterization of a cDNA encoding the

RT   cerebrovascular and the neuritic plaque amyloid peptides.";
RL   Proc. Natl. Acad. Sci. U.S.A. 84:4190-4194(1987).
RN   [15]
RP   SEQUENCE OF 286-366 FROM N.A.
RX   MEDLINE=88122640; PubMed=2893290;
RA   Tanzi R.E., McClatchey A.I., Lamperti E.D., Villa-Komaroff L.,
RA   Gusella J.F., Neve R.L.;
RT   "Protease inhibitor domain encoded by an amyloid protein precursor
RT   mRNA associated with Alzheimer's disease.";
RL   Nature 331:528-530(1988).
RN   [16]
RP   SEQUENCE OF 287-367 FROM N.A.
RX   MEDLINE=88122641; PubMed=2893291;
RA   Kitaguchi N., Takahashi Y., Tokushima Y., Shiojiri S., Ito H.;
RT   "Novel precursor of Alzheimer's disease amyloid protein shows
RT   protease inhibitory activity.";
RL   Nature 331:530-532(1988).
RN   [17]
RP   SEQUENCE OF 507-770 FROM N.A.
RC   TISSUE=Brain cortex;
RX   MEDLINE=88124954; PubMed=2893379;
RA   Zain S.B., Salim M., Chou W.G., Sajdel-Sulkowska E.M., Majocha R.E.,
RA   Marotta C.A.;
RT   "Molecular cloning of amyloid cDNA derived from mRNA of the Alzheimer
RT   disease brain: coding and noncoding regions of the fetal precursor
RT   mRNA are expressed in the cortex.";
RL   Proc. Natl. Acad. Sci. U.S.A. 85:929-933(1988).
RN   [18]
RP   SEQUENCE OF 523-555, AND COLLAGEN-BINDING DOMAIN.
RX   MEDLINE=96139497; PubMed=8576160;
RA   Beher D., Hesse L., Masters C.L., Multhaup G.;
RT   "Regulation of amyloid protein precursor (APP) binding to collagen and
RT   mapping of the binding sites on APP and collagen type I.";
RL   J. Biol. Chem. 271:1613-1620(1996).
RN   [19]
RP   SEQUENCE OF 656-737 FROM N.A.
RX   MEDLINE=89392030; PubMed=2675837;
RA   Johnstone E.M., Chaney M.O., Moore R.E., Ward K.E., Norris F.H.,
RA   Little S.P.;
RT   "Alzheimer's disease amyloid peptide is encoded by two exons and shows
RT   similarity to soybean trypsin inhibitor.";
RL   Biochem. Biophys. Res. Commun. 163:1248-1255(1989).
RN   [20]
RP   SEQUENCE OF 672-681.
RC   TISSUE=Brain cortex;
RX   MEDLINE=88035004; PubMed=3312495;
RA   Pardridge W.M., Vinters H.V., Yang J., Eisenberg J., Choi T.B.,
RA   Tourtellotte W.W., Huebner V., Shively J.E.;
RT   "Amyloid angiopathy of Alzheimer's disease: amino acid composition
RT   and partial sequence of a 4,200-dalton peptide isolated from cortical
RT   microvessels.";
RL   J. Neurochem. 49:1394-1401(1987).
RN   [21]
RP   SEQUENCE OF 674-770 FROM N.A.
RC   TISSUE=Brain;
RX   MEDLINE=87120328; PubMed=3810169;
RA   Goldgaber D., Lerman M.I., McBride O.W., Saffiotti U., Gajdusek D.C.;

RT   "Characterization and chromosomal localization of a cDNA encoding
RT   brain amyloid of Alzheimer's disease.";

   Query Match   100.0%; Score 49; DB 1; Length 770;
   Best Local Similarity   100.0%; Pred. No. 0.025;
   Matches   10; Conservative   0; Mismatches   0; Indels   0; Gaps   0;

Qy   1 SEVKMDAEFR 10
               ||||||||||
Db   667 SEVKMDAEFR 676

RESULT 9
A4_MACFA
ID   A4_MACFA   STANDARD;   PRT;   770 AA.
AC   P53601; Q95KN7;
DT   01-OCT-1996 (Rel. 34, Created)
DT   28-FEB-2003 (Rel. 41, Last sequence update)
DT   28-FEB-2003 (Rel. 41, Last annotation update)
DE   Amyloid beta A4 protein precursor (APP) (ABPP) (Alzheimer's disease
DE   amyloid protein homolog) [Contains: Soluble APP-alpha (S-APP-alpha);
DE   Soluble APP-beta (S-APP-beta); C99; Beta-amyloid protein 42 (Beta-
DE   APP42); Beta-amyloid protein 40 (Beta-APP40); C83; P3(42); P3(40);
DE   Gamma-CTF(59) (Gamma-secretase C-terminal fragment 59); Gamma-CTF(57)
DE   (Gamma-secretase C-terminal fragment 57); Gamma-CTF(50) (Gamma-
DE   secretase C-terminal fragment 50); C31].
GN   APP.
OS   Macaca fascicularis (Crab eating macaque) (Cynomolgus monkey).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC   Mammalia; Eutheria; Primates; Catarrhini; Cercopithecidae;
OC   Cercopithecinae; Macaca.
OX   NCBI_TaxID=9541;
RN   [1]
RP   SEQUENCE FROM N.A. (ISOFORMS APP695 AND APP770).
RC   TISSUE=Cerebellum;
RX   MEDLINE=91273117; PubMed=1905108;
RA   Podlisny M.B., Tolan D.R., Selkoe D.J.;
RT   "Homology of the amyloid beta protein precursor in monkey and human
RT   supports a primate model for beta amyloidosis in Alzheimer's
RT   disease.";
RL   Am. J. Pathol. 138:1423-1435(1991).
CC   -!- FUNCTION: Functions as a cell surface receptor and performs
CC   physiological functions on the surface of neurons relevant to
CC   neurite growth, neuronal adhesion and axonogenesis. Involved in
CC   cell mobility and transcription regulation through protein-protein
CC   interactions (By similarity). Can promote transcription activation
CC   through binding to APBB1/Tip60 and inhibit Notch signaling through
CC   interaction with Numb (By similarity). Couples to apoptosis-
CC   inducing pathways such as those mediated by G(O) and JIP (By
CC   similarity). Inhibits G(O) alpha ATPase activity (By similarity).
CC   Acts as a kinesin I membrane receptor, mediating the axonal
CC   transport of beta-secretase and presenilin 1 (By similarity). May
CC   be involved in copper homeostasis/oxidative stress through copper
CC   ion reduction. In vitro, copper-metallated APP induces neuronal
CC   death directly or is potentiated through Cu(II)-mediated low-
CC   density lipoprotein oxidation (By similarity). Can regulate
CC   neurite outgrowth through binding to components of the

```
CC          extracellular matrix such as heparin and collagen I and IV (By
CC          similarity). The splice isoforms that contain the BPTI domain
CC          possess protease inhibitor activity (By similarity).
CC     -!- FUNCTION: Beta-amyloid peptides are lipophilic metal chelators
CC          with metal-reducing activity. Bind transient metals such as
CC          copper, zinc and iron (By similarity).
CC     -!- FUNCTION: The gamma-CTF peptides as well as the caspase-cleaved
CC          peptides, including C31, are potent enhancers of neuronal
CC          apoptosis (By similarity).
CC     -!- SUBUNIT: Binds, via its C-terminal, to the PID domain of several
CC          cytoplasmic proteins, including APBB family members, the APBA
CC          family, MAPK8IP1, and SHC1, Numb and Dab1 (By similarity). Binding
CC          to Dab1 inhibits its serine phosphorylation (By similarity). Also
CC          interacts with GPCR-like protein BPP, FPRL1, APPBP1, IB1, KNS2
CC          (via its TPR domains) (By similarity), APPBP2 (via BaSS) and DDB1.
CC          In vitro, it binds MAPT via the MT-binding domains (By
CC          similarity). Associates with microtubules in the presence of ATP
CC          and in a kinesin-dependent manner (By similarity).
CC     -!- SUBCELLULAR LOCATION: Type I membrane protein. Cell surface
CC          protein that rapidly becomes internalized via clatherin-coated
CC          pits. During maturation, the immature APP (N-glycosylated in the
CC          endoplasmic reticulum) moves to the Golgi complex where complete
CC          maturation occurs (O-glycosylated and sulfated). After alpha-
CC          secretase cleavage, soluble APP is released into the extracellular
CC          space and the C-terminal is internalized to endosomes and
CC          lysosomes. Some APP accumulates in secretory transport vesicles
CC          leaving the late Golgi compartment and returns to the cell
CC          surface. GammaCTF(59) peptide is located to both the cytoplasm and
CC          nuclei of neurons (By similarity).
CC     -!- ALTERNATIVE PRODUCTS:
CC          Event=Alternative splicing; Named isoforms=2;
CC            Comment=Additional isoforms seem to exist;
CC          Name=APP770;
CC            IsoId=P53601-1; Sequence=Displayed;
CC          Name=APP695;
CC            IsoId=P53601-2; Sequence=VSP_000010, VSP_000011;
CC     -!- DOMAIN: The basolateral sorting signal (BaSS) is required for
CC          sorting of membrane proteins to the basolateral surface of
CC          epithelial cells (By similarity).
CC     -!- DOMAIN: The NPXY sequence motif found in many tyrosine-
CC          phosphorylated proteins is required for the specific binding of
CC          the PID domain. However additional amino acids either N- or C-
CC          terminal to the NPXY motif are often required for complete
CC          interaction. The PID domain-containing proteins which bind APP
CC          require the YENPTY motif for full interaction. These interactions
CC          are independent of phosphorylation on the terminal tyrosine
CC          residue. The NPXY site is also involved in clatherin-mediated
CC          endocytosis (By similarity).
CC     -!- PTM: Proteolytically processed under normal cellular conditions.
CC          Cleavage by alpha-secretase or alternatively by beta-secretase
CC          leads to generation and extracellular release of soluble APP
CC          peptides, S-APP-alpha and S-APP-beta, respectively, and the
CC          retention of corresponding membrane-anchored C-terminal fragments,
CC          C83 and C99. Subsequent processing of C83 by gamma-secretase
CC          yields P3 peptides. This is the major secretory pathway and is
CC          nonamyloidogenic. Alternatively, presenilin/nicastrin-mediated
CC          gamma-secretase processing of C99 releases the amyloid beta
```

```
CC        proteins, amyloid-beta 40 (Abeta40) and amyloid-beta 42 (Abeta42),
CC        major components of amyloid plaques, and the cytotoxic C-terminal
CC        fragments, gammaCTF(50), gammaCTF(57) and gammaCTF(59) (By
CC        similarity).
CC     -!- PTM: Proteolytically cleaved by caspases during neuronal apoptosis
CC        (By similarity). Cleavage at Asp-739 by either caspase-3, -8 or -9
CC        results in the production of the neurotoxic C31 peptide and the
CC        increased production of beta-amyloid peptides (By similarity).
CC     -!- PTM: N- and O-linked glycosylated (By similarity).
CC     -!- PTM: Phosphorylation in the C-terminal on tyrosine, threonine and
CC        serine residues is neuron-specific. Phosphorylation can affect APP
CC        processing, neuronal differentiation and interaction with other
CC        proteins (By similarity).
CC     -!- MISCELLANEOUS: Chelation of metal ions, notably copper, iron and
CC        zinc, can induce histidine-bridging between beta-amyloid molecules
CC        resulting in beta-amyloid-metal aggregates (By similarity).
CC        Extracellular zinc-binding increases binding of heparin to APP and
CC        inhibits collagen-binding (By similarity).
CC     -!- SIMILARITY: BELONGS TO THE APP FAMILY.
CC     -!- SIMILARITY: Contains 1 BPTI/Kunitz inhibitor domain.
CC     --------------------------------------------------------------------
CC     This SWISS-PROT entry is copyright. It is produced through a collaboration
CC     between  the Swiss Institute of Bioinformatics  and the  EMBL outstation -
CC     the European Bioinformatics Institute.  There are no  restrictions on  its
CC     use  by  non-profit  institutions as long  as its content  is  in  no  way
CC     modified and this statement is not removed.  Usage  by  and for commercial
CC     entities requires a license agreement (See http://www.isb-sib.ch/announce/
CC     or send an email to license@isb-sib.ch).
CC     --------------------------------------------------------------------
DR     EMBL; M58727; AAA36829.1; -.
DR     EMBL; M58726; AAA36828.1; -.
DR     HSSP; P05067; 1AAP.
DR     InterPro; IPR001868; A4_APP.
DR     InterPro; IPR002223; Kunitz_BPTI.
DR     Pfam; PF02177; A4_EXTRA; 1.
DR     Pfam; PF03494; Beta-APP; 1.
DR     Pfam; PF00014; Kunitz_BPTI; 1.
DR     PRINTS; PR00759; BASICPTASE.
DR     ProDom; PD000222; Kunitz_BPTI; 1.
DR     SMART; SM00006; A4_EXTRA; 1.
DR     SMART; SM00131; KU; 1.
DR     PROSITE; PS00319; A4_EXTRA; 1.
DR     PROSITE; PS00320; A4_INTRA; 1.
DR     PROSITE; PS00280; BPTI_KUNITZ_1; 1.
DR     PROSITE; PS50279; BPTI_KUNITZ_2; 1.
KW     Apoptosis; Endocytosis; Cell adhesion; Serine protease inhibitor;
KW     Coated pits; Neurone; Heparin-binding; Metal-binding; Copper; Iron;
KW     Zinc; Signal; Transmembrane; Glycoprotein; Phosphorylation;
KW     Proteoglycan; Alternative splicing; Amyloid.
FT     SIGNAL          1      17        BY SIMILARITY.
FT     CHAIN          18     770        AMYLOID BETA A4 PROTEIN.
FT     CHAIN          18     687        SOLUBLE APP-ALPHA (POTENTIAL).
FT     CHAIN          18     671        SOLUBLE APP-BETA (POTENTIAL).
FT     CHAIN         672     770        C99 (POTENTIAL).
FT     CHAIN         672     713        BETA-AMYLOID PROTEIN 42 (POTENTIAL).
FT     CHAIN         672     711        BETA-AMYLOID PROTEIN 40 (POTENTIAL).
FT     CHAIN         688     770        C83 (POTENTIAL).
```

```
FT    CHAIN       688     713     P3(42) (POTENTIAL).
FT    CHAIN       688     711     P3(40) (POTENTIAL).
FT    CHAIN       712     770     GAMMA-CTF(59) (POTENTIAL).
FT    CHAIN       714     770     GAMMA-CTF(57) (POTENTIAL).
FT    CHAIN       721     770     GAMMA-CTF(50) (POTENTIAL).
FT    CHAIN       740     770     C31 (POTENTIAL).
FT    DOMAIN       18     699     EXTRACELLULAR (POTENTIAL).
FT    TRANSMEM    700     723     POTENTIAL.
FT    DOMAIN      724     770     CYTOPLASMIC (POTENTIAL).
FT    DOMAIN       96     110     HEPARIN-BINDING (BY SIMILARITY).
FT    DOMAIN      181     188     ZINC-BINDING (BY SIMILARITY).
FT    DOMAIN      291     341     BPTI/KUNITZ INHIBITOR.
FT    DOMAIN      391     423     HEPARIN-BINDING (BY SIMILARITY).
FT    DOMAIN      491     522     HEPARIN-BINDING (BY SIMILARITY).
FT    DOMAIN      523     540     COLLAGEN-BINDING (BY SIMILARITY).
FT    DOMAIN      732     751     INTERACTION WITH G(O)-ALPHA
FT                                (BY SIMILARITY).
FT    DOMAIN      230     260     ASP/GLU-RICH (ACIDIC).
FT    DOMAIN      274     280     POLY-THR.
FT    SITE        144     144     REQUIRED FOR COPPER(II) REDUCTION
FT                                (BY SIMILARITY).
FT    ACT_SITE    301     302     REACTIVE BOND (BY SIMILARITY).
FT    SITE        671     672     CLEAVAGE (BY BETA-SECRETASE)
FT                                (BY SIMILARITY).
FT    SITE        672     673     CLEAVAGE (BY CASPASE-6) (BY SIMILARITY).
FT    SITE        687     688     CLEAVAGE (BY ALPHA-SECRETASE)
FT                                (BY SIMILARITY).
FT    SITE        704     704     IMPLICATED IN FREE RADICAL PROPAGATION
FT                                (BY SIMILARITY).
FT    SITE        706     706     INVOLVED IN OXIDATIVE REACTIONS
FT                                (BY SIMILARITY).
FT    SITE        711     712     CLEAVAGE (BY GAMMA-SECRETASE; SITE 1)
FT                                (BY SIMILARITY).
FT    SITE        713     714     CLEAVAGE (BY GAMMA-SECRETASE; SITE 2)
FT                                (BY SIMILARITY).
FT    SITE        720     721     CLEAVAGE (BY GAMMA-SECRETASE; SITE 3)
FT                                (BY SIMILARITY).
FT    SITE        724     734     BASOLATERAL SORTING SIGNAL
FT                                (BY SIMILARITY).
FT    SITE        739     740     CLEAVAGE (BY CASPASES-3,-6,-8 OR -9)
FT                                (BY SIMILARITY).
FT    SITE        757     760     ENDOCYTOSIS SIGNAL.
FT    SITE        759     762     NPXY MOTIF.

    Query Match              100.0%;  Score 49;  DB 1;  Length 770;
    Best Local Similarity    100.0%;  Pred. No. 0.025;
    Matches   10;  Conservative   0;  Mismatches    0;  Indels   0;  Gaps    0;

Qy        1 SEVKMDAEFR 10
            ||||||||||
Db      667 SEVKMDAEFR 676


RESULT 10
A4_PIG
ID    A4_PIG          STANDARD;       PRT;    770 AA.
AC    P79307; Q29023; Q9TUI0;
```

DE   Amyloid beta A4 protein precursor (APP) (ABPP) (Alzheimer's disease
DE   amyloid protein homolog) [Contains: Soluble APP-alpha (S-APP-alpha);
DE   Soluble APP-beta (S-APP-beta); C99; Beta-amyloid protein 42 (Beta-
DE   APP42); Beta-amyloid protein 40 (Beta-APP40); C83; P3(42); P3(40);
DE   Gamma-CTF(59) (Gamma-secretase C-terminal fragment 59); Gamma-CTF(57)
DE   (Gamma-secretase C-terminal fragment 57); Gamma-CTF(50) (Gamma-
DE   secretase C-terminal fragment 50); C31].
OS   Sus scrofa (Pig).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC   Mammalia; Eutheria; Cetartiodactyla; Suina; Suidae; Sus.
OX   NCBI_TaxID=9823;
RN   [1]
RP   SEQUENCE FROM N.A.
RA   Kimura A., Takahashi T.;
RT   "Amyloid precursor protein 770.";
RL   Submitted (SEP-1999) to the EMBL/GenBank/DDBJ databases.
RN   [2]
RP   SEQUENCE OF 1-136 FROM N.A.
RC   TISSUE=Small intestine;
RA   Winteroe A.K., Fredholm M.;
RT   "Evaluation and characterization of a porcine small intestine cDNA
RT   library.";
RL   Submitted (JAN-1997) to the EMBL/GenBank/DDBJ databases.
RN   [3]
RP   SEQUENCE OF 667-723 FROM N.A.
RC   TISSUE=Brain;
RX   MEDLINE=92017079; PubMed=1656157;
RA   Johnstone E.M., Chaney M.O., Norris F.H., Pascual R., Little S.P.;
RT   "Conservation of the sequence of the Alzheimer's disease amyloid
RT   peptide in dog, polar bear and five other mammals by cross-species
RT   polymerase chain reaction analysis.";
RL   Brain Res. Mol. Brain Res. 10:299-305(1991).
CC   -!- FUNCTION: Functions as a cell surface receptor and performs
CC   physiological functions on the surface of neurons relevant to
CC   neurite growth, neuronal adhesion and axonogenesis. Involved in
CC   cell mobility and transcription regulation through protein-protein
CC   interactions (By similarity). Can promote transcription activation
CC   through binding to APBB1/Tip60 and inhibit Notch signaling through
CC   interaction with Numb (By similarity). Couples to apoptosis-
CC   inducing pathways such as those mediated by G(O) and JIP (By
CC   similarity). Inhibits G(0) alpha ATPase activity (By similarity).
CC   Acts as a kinesin I membrane receptor, mediating the axonal
CC   transport of beta-secretase and presenilin 1 (By similarity). May
CC   be involved in copper homeostasis/oxidative stress through copper
CC   ion reduction (By similarity). In vitro, copper-metallated APP
CC   induces neuronal death directly or is potentiated through Cu(II)-
CC   mediated low-density lipoprotein oxidation (By similarity). Can
CC   regulate neurite outgrowth through binding to components of the
CC   extracellular matrix such as heparin and collagen I and IV (By
CC   similarity).
CC   -!- FUNCTION: Beta-amyloid peptides are lipophilic metal chelators
CC   with metal-reducing activity. Bind transient metals such as
CC   copper, zinc and iron (By similarity).
CC   -!- FUNCTION: The gamma-CTF peptides as well as the caspase-cleaved

```
CC          peptides, including C31, are potent enhancers of neuronal
CC          apoptosis (By similarity).
CC     -!- SUBUNIT: Binds, via its C-terminal, to the PID domain of several
CC          cytoplasmic proteins, including APBB family members, the APBA
CC          family, MAPK8IP1, and SHC1, Numb and Dab1 (By similarity). Binding
CC          to Dab1 inhibits its serine phosphorylation (By similarity). Also
CC          interacts with GPCR-like protein BPP, FPRL1, APPBP1, IB1, KNS2
CC          (via its TPR domains) (By similarity), APPBP2 (via BaSS) and DDB1.
CC          In vitro, it binds MAPT via the MT-binding domains (By
CC          similarity). Associates with microtubules in the presence of ATP
CC          and in a kinesin-dependent manner (By similarity).
CC     -!- SUBCELLULAR LOCATION: Type I membrane protein. Cell surface
CC          protein that rapidly becomes internalized via clatherin-coated
CC          pits. During maturation, the immature APP (N-glycosylated in the
CC          endoplasmic reticulum) moves to the Golgi complex where complete
CC          maturation occurs (O-glycosylated and sulfated). After alpha-
CC          secretase cleavage, soluble APP is released into the extracellular
CC          space and the C-terminal is internalized to endosomes and
CC          lysosomes. Some APP accumulates in secretory transport vesicles
CC          leaving the late Golgi compartment and returns to the cell
CC          surface. GammaCTF(59) peptide is located to both the cytoplasm and
CC          nuclei of neurons (By similarity).
CC     -!- DOMAIN: The basolateral sorting signal (BaSS) is required for
CC          sorting of membrane proteins to the basolateral surface of
CC          epithelial cells (By similarity).
CC     -!- DOMAIN: The NPXY sequence motif found in many tyrosine-
CC          phosphorylated proteins is required for the specific binding of
CC          the PID domain. However additional amino acids either N- or C-
CC          terminal to the NPXY motif are often required for complete
CC          interaction. The PID domain-containing proteins which bind APP
CC          require the YENPTY motif for full interaction. These interactions
CC          are independent of phosphorylation on the terminal tyrosine
CC          residue. The NPXY site is also involved in clatherin-mediated
CC          endocytosis (By similarity).
CC     -!- PTM: Proteolytically processed under normal cellular conditions.
CC          Cleavage by alpha-secretase or alternatively by beta-secretase
CC          leads to generation and extracellular release of soluble APP
CC          peptides, S-APP-alpha and S-APP-beta, respectively, and the
CC          retention of corresponding membrane-anchored C-terminal fragments,
CC          C83 and C99. Subsequent processing of C83 by gamma-secretase
CC          yields P3 peptides. This is the major secretory pathway and is
CC          nonamyloidogenic. Alternatively, presenilin/nicastrin-mediated
CC          gamma-secretase processing of C99 releases the amyloid beta
CC          proteins, amyloid-beta 40 (Abeta40) and amyloid-beta 42 (Abeta42),
CC          major components of amyloid plaques, and the cytotoxic C-terminal
CC          fragments, gammaCTF(50), gammaCTF(57) and gammaCTF(59) (By
CC          similarity).
CC     -!- PTM: Proteolytically cleaved by caspases during neuronal apoptosis
CC          (By similarity). Cleavage at Asp-739 by either caspase-3, -8 or -9
CC          results in the production of the neurotoxic C31 peptide and the
CC          increased production of beta-amyloid peptides (By similarity).
CC     -!- PTM: N- and O-linked glycosylated (By similarity).
CC     -!- PTM: Phosphorylation in the C-terminal on tyrosine, threonine and
CC          serine residues is neuron-specific. Phosphorylation can affect APP
CC          processing, neuronal differentiation and interaction with other
CC          proteins (By similarity).
CC     -!- PTM: Extracellular binding and reduction of copper, results in a
```

```
CC          corresponding oxidation of Cys-144 and Cys-158, and the formation
CC          of a disulfide bond (By similarity).
CC     -!- MISCELLANEOUS: Chelation of metal ions, notably copper, iron and
CC          zinc, can induce histidine-bridging between beta-amyloid molecules
CC          resulting in beta-amyloid-metal aggregates (By similarity).
CC          Extracellular zinc-binding increases binding of heparin to APP and
CC          inhibits collagen-binding (By similarity).
CC     -!- SIMILARITY: BELONGS TO THE APP FAMILY.
CC     -!- SIMILARITY: Contains 1 BPTI/Kunitz inhibitor domain.
CC     --------------------------------------------------------------------------
CC     This SWISS-PROT entry is copyright. It is produced through a collaboration
CC     between  the Swiss Institute of Bioinformatics  and the  EMBL outstation -
CC     the European Bioinformatics Institute.  There are no  restrictions on  its
CC     use  by  non-profit  institutions as long  as its content  is  in  no  way
CC     modified and this statement is not removed.  Usage  by  and for commercial
CC     entities requires a license agreement (See http://www.isb-sib.ch/announce/
CC     or send an email to license@isb-sib.ch).
CC     --------------------------------------------------------------------------
DR     EMBL; AB032550; BAA84580.1; -.
DR     EMBL; Z84022; CAB06313.1; -.
DR     EMBL; X56127; CAA39592.1; -.
DR     HSSP; P05067; 1AAP.
DR     InterPro; IPR008155; A4_APP.
DR     InterPro; IPR008154; A4_extra.
DR     InterPro; IPR001255; Beta-APP.
DR     InterPro; IPR002223; Kunitz_BPTI.
DR     Pfam; PF02177; A4_EXTRA; 1.
DR     PRINTS; PR00203; AMYLOIDA4.
DR     PRINTS; PR00759; BASICPTASE.
DR     ProDom; PD000222; Kunitz_BPTI; 1.
DR     SMART; SM00006; A4_EXTRA; 1.
DR     SMART; SM00131; KU; 1.
DR     PROSITE; PS00319; A4_EXTRA; 1.
DR     PROSITE; PS00320; A4_INTRA; 1.
DR     PROSITE; PS00280; BPTI_KUNITZ_1; 1.
DR     PROSITE; PS50279; BPTI_KUNITZ_2; 1.
KW     Apoptosis; Endocytosis; Cell adhesion; Serine protease inhibitor;
KW     Coated pits; Neurone; Heparin-binding; Metal-binding; Copper; Iron;
KW     Zinc; Signal; Transmembrane; Glycoprotein; Phosphorylation;
KW     Amyloid.
FT     SIGNAL          1      17       BY SIMILARITY.
FT     CHAIN          18     770       AMYLOID BETA A4 PROTEIN.
FT     CHAIN          18     687       SOLUBLE APP-ALPHA (POTENTIAL).
FT     CHAIN          18     671       SOLUBLE APP-BETA (POTENTIAL).
FT     CHAIN         672     770       C99 (BY SIMILARITY).
FT     CHAIN         672     713       BETA-AMYLOID PROTEIN 42 (BY SIMILARITY).
FT     CHAIN         672     711       BETA-AMYLOID PROTEIN 40 (BY SIMILARITY).
FT     CHAIN         688     770       C83 (BY SIMILARITY).
FT     CHAIN         688     713       P3(42) (BY SIMILARITY).
FT     CHAIN         688     711       P3(40) (BY SIMILARITY).
FT     CHAIN         712     770       GAMMA-CTF(59).
FT     CHAIN         714     770       GAMMA-CTF(57).
FT     CHAIN         721     770       GAMMA-CTF(50) (BY SIMILARITY).
FT     CHAIN         740     770       C31 (DURING APOPTOSIS) (BY SIMILARITY).
FT     DOMAIN         18     699       EXTRACELLULAR (POTENTIAL).
FT     TRANSMEM      700     723       POTENTIAL.
FT     DOMAIN        724     770       CYTOPLASMIC (POTENTIAL).
```

```
FT   DOMAIN         96    110   HEPARIN-BINDING (BY SIMILARITY).
FT   DOMAIN        135    155   COPPER-BINDING (BY SIMILARITY).
FT   DOMAIN        181    188   ZINC-BINDING (BY SIMILARITY).
FT   DOMAIN        291    341   BPTI/KUNITZ INHIBITOR.
FT   DOMAIN        391    423   HEPARIN-BINDING (BY SIMILARITY).
FT   DOMAIN        491    522   HEPARIN-BINDING (BY SIMILARITY).
FT   DOMAIN        523    540   COLLAGEN-BINDING (BY SIMILARITY).
FT   DOMAIN        732    751   INTERACTION WITH G(O)-ALPHA (BY
FT                              SIMILARITY).
FT   DOMAIN        230    260   ASP/GLU-RICH (ACIDIC).
FT   DOMAIN        274    280   POLY-THR.
FT   SITE          144    144   REQUIRED FOR COPPER(II) REDUCTION
FT                              (BY SIMILARITY).
FT   ACT_SITE      301    302   REACTIVE BOND (BY SIMILARITY).
FT   SITE          671    672   CLEAVAGE (BY BETA-SECRETASE)
FT                              (BY SIMILARITY).
FT   SITE          672    673   CLEAVAGE (BY CASPASE-6) (BY SIMILARITY).
FT   SITE          687    688   CLEAVAGE (BY ALPHA-SECRETASE)
FT                              (BY SIMILARITY).
FT   SITE          704    704   IMPLICATED IN FREE RADICAL PROPAGATION
FT                              (BY SIMILARITY).
FT   SITE          706    706   INVOLVED IN OXIDATIVE REACTIONS
FT                              (BY SIMILARITY).
FT   SITE          711    712   CLEAVAGE (BY GAMMA-SECRETASE; SITE 1)
FT                              (BY SIMILARITY).
FT   SITE          713    714   CLEAVAGE (BY GAMMA-SECRETASE; SITE 2)
FT                              (BY SIMILARITY).

     Query Match          100.0%;  Score 49;  DB 1;  Length 770;
     Best Local Similarity  100.0%;  Pred. No. 0.025;
     Matches    10;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy        1 SEVKMDAEFR 10
            | | | | | | | | | |
Db      667 SEVKMDAEFR 676


RESULT 11
A4_MOUSE
ID   A4_MOUSE        STANDARD;      PRT;     770 AA.
AC   P12023; P97487; P97942; Q99K32;
DT   01-OCT-1989 (Rel. 12, Created)
DT   15-SEP-2003 (Rel. 42, Last sequence update)
DT   15-SEP-2003 (Rel. 42, Last annotation update)
DE   Amyloid beta A4 protein precursor (APP) (ABPP) (Alzheimer's disease
DE   amyloid protein homolog) (Amyloidogenic glycoprotein) (AG) [Contains:
DE   Soluble APP-alpha (S-APP-alpha); Soluble APP-beta (S-APP-beta); C99
DE   (APP-C99); Beta-amyloid protein 42 (Beta-APP42); Beta-amyloid protein
DE   40 (Beta-APP40); C83; P3(42); P3(40); Gamma-CTF(59) (Gamma-secretase
DE   C-terminal fragment 59) (Amyloid intracellular domain 59) (AID(59))
DE   (APP-C59); Gamma-CTF(57) (Gamma-secretase C-terminal fragment 57)
DE   (Amyloid intracellular domain 57) (AID(57)) (APP-C57); Gamma-CTF(50)
DE   (Gamma-secretase C-terminal fragment 50) (Amyloid intracellular domain
DE   50) (AID(50)); C31].
GN   APP.
OS   Mus musculus (Mouse).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
```

OC   Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Mus.
OX   NCBI_TaxID=10090;
RN   [1]
RP   SEQUENCE FROM N.A. (ISOFORM APP695).
RC   TISSUE=Brain;
RX   MEDLINE=88106489; PubMed=3322280;
RA   Yamada T., Sasaki H., Furuya H., Miyata T., Goto I., Sakaki Y.;
RT   "Complementary DNA for the mouse homolog of the human amyloid beta
RT   protein precursor.";
RL   Biochem. Biophys. Res. Commun. 149:665-671(1987).
RN   [2]
RP   REVISIONS.
RA   Yamada T.;
RL   Submitted (MAR-1988) to the EMBL/GenBank/DDBJ databases.
RN   [3]
RP   SEQUENCE FROM N.A. (ISOFORM APP695).
RC   STRAIN=BALB/c; TISSUE=Brain;
RX   MEDLINE=92096458; PubMed=1756177;
RA   de Strooper B., van Leuven F., van den Berghe H.;
RT   "The amyloid beta protein precursor or proteinase nexin II from mouse
RT   is closer related to its human homolog than previously reported.";
RL   Biochim. Biophys. Acta 1129:141-143(1991).
RN   [4]
RP   SEQUENCE FROM N.A. (ISOFORM APP695).
RC   STRAIN=SAMP8; TISSUE=Hippocampus;
RX   PubMed=11235921;
RA   Kumar V.B., Vyas K., Franko M., Choudhary V., Buddhiraju C.,
RA   Alvarez J., Morley J.E.;
RT   "Molecular cloning, expression, and regulation of hippocampal amyloid
RT   precursor protein of senescence accelerated mouse (SAMP8).";
RL   Biochem. Cell Biol. 79:57-67(2001).
RN   [5]
RP   SEQUENCE OF 1-19 FROM N.A.
RX   MEDLINE=92209998; PubMed=1555768;
RA   Izumi R., Yamada T., Yoshikai S.I., Sasaki H., Hattori M.,
RA   Sakai Y.;
RT   "Positive and negative regulatory elements for the expression of the
RT   Alzheimer's disease amyloid precursor-encoding gene in mouse.";
RL   Gene 112:189-195(1992).
RN   [6]
RP   PARTIAL SEQUENCE FROM N.A. (ISOFORM APP770).
RC   TISSUE=Breast tumor;
RX   MEDLINE=22388257; PubMed=12477932;
RA   Strausberg R.L., Feingold E.A., Grouse L.H., Derge J.G.,
RA   Klausner R.D., Collins F.S., Wagner L., Shenmen C.M., Schuler G.D.,
RA   Altschul S.F., Zeeberg B., Buetow K.H., Schaefer C.F., Bhat N.K.,
RA   Hopkins R.F., Jordan H., Moore T., Max S.I., Wang J., Hsieh F.,
RA   Diatchenko L., Marusina K., Farmer A.A., Rubin G.M., Hong L.,
RA   Stapleton M., Soares M.B., Bonaldo M.F., Casavant T.L., Scheetz T.E.,
RA   Brownstein M.J., Usdin T.B., Toshiyuki S., Carninci P., Prange C.,
RA   Raha S.S., Loquellano N.A., Peters G.J., Abramson R.D., Mullahy S.J.,
RA   Bosak S.A., McEwan P.J., McKernan K.J., Malek J.A., Gunaratne P.H.,
RA   Richards S., Worley K.C., Hale S., Garcia A.M., Gay L.J., Hulyk S.W.,
RA   Villalon D.K., Muzny D.M., Sodergren E.J., Lu X., Gibbs R.A.,
RA   Fahey J., Helton E., Ketteman M., Madan A., Rodrigues S., Sanchez A.,
RA   Whiting M., Madan A., Young A.C., Shevchenko Y., Bouffard G.G.,
RA   Blakesley R.W., Touchman J.W., Green E.D., Dickson M.C.,

RA   Rodriguez A.C., Grimwood J., Schmutz J., Myers R.M.,
RA   Butterfield Y.S.N., Krzywinski M.I., Skalska U., Smailus D.E.,
RA   Schnerch A., Schein J.E., Jones S.J.M., Marra M.A.;
RT   "Generation and initial analysis of more than 15,000 full-length human
RT   and mouse cDNA sequences.";
RL   Proc. Natl. Acad. Sci. U.S.A. 99:16899-16903(2002).
RN   [7]
RP   SEQUENCE OF 281-380 FROM N.A., AND ALTERNATIVE SPLICING.
RC   TISSUE=Brain, and Kidney;
RX   MEDLINE=89149813; PubMed=2493250;
RA   Yamada T., Sasaki H., Dohura K., Goto I., Sakaki Y.;
RT   "Structure and expression of the alternatively-spliced forms of mRNA
RT   for the mouse homolog of Alzheimer's disease amyloid beta protein
RT   precursor.";
RL   Biochem. Biophys. Res. Commun. 158:906-912(1989).
RN   [8]
RP   SEQUENCE OF 289-364 FROM N.A.
RC   STRAIN=CD-1; TISSUE=Placenta;
RX   MEDLINE=89345111; PubMed=2569710;
RA   Fukuchi K., Martin G.M., Deeb S.S.;
RT   "Sequence of the protease inhibitor domain of the A4 amyloid protein
RT   precursor of Mus domesticus.";
RL   Nucleic Acids Res. 17:5396-5396(1989).
RN   [9]
RP   SEQUENCE OF 656-737 FROM N.A.
RC   STRAIN=129/Sv;
RA   Wragg M.A., Busfield F., Duff K., Korenblat K., Capecchi M.,
RA   Loring J.F., Goate A.M.;
RT   "Introduction of six mutations into the mouse genome using 'Hit and
RT   Run' gene-targeting: introduction of familial Alzheimer's disease
RT   mutations into the mouse amyloid precursor protein gene and
RT   humanization of the A-beta fragment.";
RL   Submitted (DEC-1996) to the EMBL/GenBank/DDBJ databases.
RN   [10]
RP   TISSUE SPECIFICITY OF ALTERNATIVE SPLICED FORMS.
RX   PubMed=8510506;
RA   Sola C., Mengod G., Ghetti B., Palacios J.M., Triarhou L.C.;
RT   "Regional distribution of the alternatively spliced isoforms of beta
RT   APP RNA transcript in the brain of normal, heterozygous and
RT   homozygous weaver mutant mice as revealed by in situ hybridization
RT   histochemistry.";
RL   Brain Res. Mol. Brain Res. 17:340-346(1993).
RN   [11]
RP   INTERACTION WITH KNS2.
RX   PubMed=11144355;
RA   Kamal A., Stokin G.B., Yang Z., Xia C.-H., Goldstein L.S.;
RT   "Axonal transport of amyloid precursor protein is mediated by direct
RT   binding to the kinesin light chain subunit of kinesin-I.";
RL   Neuron 28:449-459(2000).
RN   [12]
RP   C-TERMINAL PROTEIN-PROTEIN INTERACTIONS, AND MUTAGENESIS OF TYR-728;
RP   THR-743; TYR-757; ASN-759 AND TYR-762.
RX   MEDLINE=21408156; PubMed=11517249;
RA   Matsuda S., Yasukawa T., Homma Y., Ito Y., Niikura T., Hiraki T.,
RA   Hirai S., Ohno S., Kita Y., Kawasumi M., Kouyama K., Yamamoto T.,
RA   Kyriakis J.M., Nishimoto I.;
RT   "C-jun N-terminal kinase (JNK)-interacting protein-1b/islet-brain-1

RT   scaffolds Alzheimer's amyloid precursor protein with JNK.";
RL   J. Neurosci. 21:6597-6607(2001).
RN   [13]
RP   INTERACTION WITH MAPK8IP1, AND PHOSPHORYLATION.
RX   MEDLINE=22028091; PubMed=11912189;
RA   Taru H., Iijima K.-I., Hase M., Kirino Y., Yagi Y., Suzuki T.;
RT   "Interaction of Alzheimer's beta-amyloid precursor family proteins
RT   with scaffold proteins of the JNK signaling cascade.";
RL   J. Biol. Chem. 277:20070-20078(2002).
RN   [14]
RP   INTERACTION OF CTF PEPTIDES WITH NUMB.
RX   PubMed=12011466;
RA   Roncarati R., Sestan N., Scheinfeld M.H., Berechid B.E., Lopez P.A.,
RA   Meucci O., McGlade J.C., Rakic P., D'Adamio L.;
RT   "The gamma-secretase-generated intracellular domain of beta-amyloid
RT   precursor protein binds Numb and inhibits Notch signaling.";
RL   Proc. Natl. Acad. Sci. U.S.A. 99:7102-7107(2002).
RN   [15]
RP   GAMMA-SECRETASE PROCESSING, AND INTERACTION WITH APBB1.
RX   PubMed=11553691;
RA   Cupers P., Orlans I., Craessaerts K., Annaert W., De Strooper B.;
RT   "The amyloid precursor protein (APP)-cytoplasmic fragment generated by
RT   gamma-secretase is rapidly degraded but distributes partially in a
RT   nuclear fraction of neurones in culture.";
RL   J. Neurochem. 78:1168-1178(2001).
CC   -!- FUNCTION: Functions as a cell surface receptor and performs
CC   physiological functions on the surface of neurons relevant to
CC   neurite growth, neuronal adhesion and axonogenesis. Involved in
CC   cell mobility and transcription regulation through protein-protein
CC   interactions. Can promote transcription activation through binding
CC   to APBB1/Tip60 and inhibit Notch signaling through interaction
CC   with Numb. Couples to apoptosis-inducing pathways such as those
CC   mediated by G(O) and JIP. Inhibits G(O) alpha ATPase activity (By
CC   similarity). Acts as a kinesin I membrane receptor, mediating the
CC   axonal transport of beta-secretase and presenilin 1. May be
CC   involved in copper homeostasis/oxidative stress through copper ion
CC   reduction. Can regulate neurite outgrowth through binding to
CC   components of the extracellular matrix such as heparin and
CC   collagen I and IV (By similarity). The splice isoforms that
CC   contain the BPTI domain possess protease inhibitor activity (By
CC   similarity).
CC   -!- FUNCTION: Beta-amyloid peptides are lipophilic metal chelators
CC   with metal-reducing activity. Bind transient metals such as
CC   copper, zinc and iron. Rat and mouse beta-amyloid peptides bind
CC   only weakly transient metals and have little reducing activity due
CC   to substitutions of transient metal chelating residues. Beta-APP42
CC   may activate mononuclear phagocytes in the brain and elicit
CC   inflammatory responses. Promotes both tau aggregation and TPK II-
CC   mediated phosphorylation (By similarity).
CC   -!- FUNCTION: The gamma-CTF peptides as well as the caspase-cleaved
CC   peptides, including C31, are potent enhancers of neuronal
CC   apoptosis.
CC   -!- SUBUNIT: Binds, via its C-terminal, to the PID domain of several
CC   cytoplasmic proteins, including APBB family members, the APBA
CC   family, MAPK8IP1, SHC1, Numb and Dab1. Binding to Dab1 inhibits
CC   its serine phosphorylation. Also interacts with GPCR-like protein
CC   BPP, FPRL1, APPBP1, IB1, KNS2 (via its TPR domains), APPBP2 (via

Query Match   89.8%;   Score 44;   DB 1;   Length 770;
Best Local Similarity   100.0%;   Pred. No. 0.26;
Matches   9;   Conservative   0;   Mismatches   0;   Indels   0;   Gaps   0;

Qy   1 SEVKMDAEF 9
            | | | | | | | | |
Db   667 SEVKMDAEF 675

RESULT 12
A4_RAT
ID   A4_RAT   STANDARD;   PRT;   770 AA.
AC   P08592;
DT   01-AUG-1988 (Rel. 08, Created)
DT   01-DEC-1992 (Rel. 24, Last sequence update)
DT   15-SEP-2003 (Rel. 42, Last annotation update)
DE   Amyloid beta A4 protein precursor (APP) (Alzheimer's disease amyloid
DE   protein homolog) (Amyloidogenic glycoprotein) (AG) [Contains: Soluble
DE   APP-alpha (S-APP-alpha); Soluble APP-beta (S-APP-beta); C99; Beta-
DE   amyloid protein 42 (Beta-APP42); Beta-amyloid protein 40 (Beta-APP40);
DE   C83; P3(42); P3(40); Gamma-CTF(59) (Gamma-secretase C-terminal
DE   fragment 59); Gamma-CTF(57) (Gamma-secretase C-terminal fragment 57);
DE   Gamma-CTF(50) (Gamma-secretase C-terminal fragment 50); C31].
GN   APP.
OS   Rattus norvegicus (Rat).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC   Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Rattus.
OX   NCBI_TaxID=10116;
RN   [1]
RP   SEQUENCE FROM N.A. (ISOFORM APP695).
RC   TISSUE=Brain;
RX   MEDLINE=88312583; PubMed=2900758;
RA   Shivers B.D., Hilbich C., Multhaup G., Salbaum J.M., Beyreuther K.,
RA   Seeburg P.H.;
RT   "Alzheimer's disease amyloidogenic glycoprotein: expression pattern
RT   in rat brain suggests a role in cell contact.";
RL   EMBO J. 7:1365-1370(1988).
RN   [2]
RP   SEQUENCE OF 289-364 FROM N.A.
RC   TISSUE=Liver;
RX   MEDLINE=89183625; PubMed=2648331;
RA   Kang J., Mueller-Hill B.;
RT   "The sequence of the two extra exons in rat preA4.";
RL   Nucleic Acids Res. 17:2130-2130(1989).
RN   [3]

RP   SEQUENCE OF 720-730, AND MASS SPECTROMETRY.
RX   PubMed=11483588;
RA   Gu Y., Misonou H., Sato T., Dohmae N., Takio K., Ihara Y.;
RT   "Distinct intramembrane cleavage of the beta-amyloid precursor protein
RT   family resembling gamma-secretase-like cleavage of Notch.";
RL   J. Biol. Chem. 276:35235-35238(2001).
RN   [4]
RP   ALTERNATIVE SPLICING.
RX   PubMed=8624099;
RA   Sandbrink R., Masters C.L., Beyreuther K.;
RT   "APP gene family. Alternative splicing generates functionally related
RT   isoforms.";
RL   Ann. N.Y. Acad. Sci. 777:281-287(1996).
RN   [5]
RP   TISSUE SPECIFICITY OF APPICAN.
RX   PubMed=7744833;
RA   Shioi J., Pangalos M.N., Ripellino J.A., Vassilacopoulou D.,
RA   Mytilineou C., Margolis R.U., Robakis N.K.;
RT   "The Alzheimer amyloid precursor proteoglycan (appican) is present in
RT   brain and is produced by astrocytes but not by neurons in primary
RT   neural cultures.";
RL   J. Biol. Chem. 270:11839-11844(1995).
RN   [6]
RP   TISSUE SPECIFICITY OF ISOFORMS.
RX   PubMed=8996834;
RA   Sandbrink R., Monning U., Masters C.L., Beyreuther K.;
RT   "Expression of the APP gene family in brain cells, brain development
RT   and aging.";
RL   Gerontology 43:119-131(1997).
RN   [7]
RP   INTERACTION WITH DDB1, AND MUTAGENESIS OF TYR-757; ASN-759 AND
RP   TYR-762.
RX   PubMed=9930726;
RA   Watanabe T., Sukegawa J., Tomita S., Iijima K.-I., Oguchi S.,
RA   Suzuki T., Nairn A.C., Greengard P.;
RT   "A 127-kDa protein (UV-DDB) binds to the cytoplasmic domain of the
RT   Alzheimer's amyloid precursor protein.";
RL   J. Neurochem. 72:549-556(1999).
RN   [8]
RP   INTERACTION WITH GNAO1, AND MUTAGENESIS OF HIS-732 AND HIS-733.
RX   PubMed=10024358;
RA   Brouillet E., Trembleau A., Galanaud D., Volovitch M., Bouillot C.,
RA   Valenza C., Prochiantz A., Allinquant B.;
RT   "The amyloid precursor protein interacts with Go heterotrimeric
RT   protein within a cell compartment specialized in signal
RT   transduction.";
RL   J. Neurosci. 19:1717-1727(1999).
RN   [9]
RP   CHARACTERISTICS OF APPICAN, AND MUTAGENESIS OF SER-656.
RX   MEDLINE=95256193; PubMed=7737970;
RA   Pangalos M.N., Efthimiopoulos S., Shioi J., Robakis N.K.;
RT   "The chondroitin sulfate attachment site of appican is formed by
RT   splicing out exon 15 of the amyloid precursor gene.";
RL   J. Biol. Chem. 270:10388-10391(1995).
RN   [10]
RP   BETA-AMYLOID METAL-BINDING.
RX   PubMed=10386999;

RA   Huang X., Atwood C.S., Hartshorn M.A., Multhaup G., Goldstein L.E.,
RA   Scarpa R.C., Cuajungco M.P., Gray D.N., Lim J., Moir R.D., Tanzi R.E.,
RA   Bush A.I.;
RT   "The A beta peptide of Alzheimer's disease directly produces hydrogen
RT   peroxide through metal ion reduction.";
RL   Biochemistry 38:7609-7616(1999).
RN   [11]
RP   BETA-AMYLOID ZINC BINDING.
RX   MEDLINE=99343552; PubMed=10413512;
RA   Liu S.T., Howlett G., Barrow C.J.;
RT   "Histidine-13 is a crucial residue in the zinc ion-induced aggregation
RT   of the A beta peptide of Alzheimer's disease.";
RL   Biochemistry 38:9373-9378(1999).
RN   [12]
RP   IMPORTANCE OF GLY-704 IN FREE RADICAL PROPAGATION, AND MUTAGENESIS OF
RP   GLY-704.
RX   PubMed=11959460;
RA   Kanski J., Varadarajan S., Aksenova M., Butterfield D.A.;
RT   "Role of glycine-33 and methionine-35 in Alzheimer's amyloid beta-
RT   peptide 1-42-associated oxidative stress and neurotoxicity.";
RL   Biochim. Biophys. Acta 1586:190-198(2001).
RN   [13]
RP   PHOSPHORYLATION.
RX   PubMed=9085254;
RA   Oishi M., Nairn A.C., Czernik A.J., Lim G.S., Isohara T., Gandy S.E.,
RA   Greengard P., Suzuki T.;
RT   "The cytoplasmic domain of Alzheimer's amyloid precursor protein is
RT   phosphorylated at Thr654, Ser655, and Thr668 in adult rat brain and
RT   cultured cells.";
RL   Mol. Med. 3:111-123(1997).
RN   [14]
RP   PHOSPHORYLATION ON SER-730.
RX   PubMed=10329382;
RA   Isohara T., Horiuchi A., Watanabe T., Ando K., Czernik A.J., Uno I.,
RA   Greengard P., Nairn A.C., Suzuki T.;
RT   "Phosphorylation of the cytoplasmic domain of Alzheimer's beta-amyloid
RT   precursor protein at Ser655 by a novel protein kinase.";
RL   Biochem. Biophys. Res. Commun. 258:300-305(1999).
RN   [15]
RP   PHOSPHORYLATION, INDUCTION, SUBCELLULAR LOCATION, AND MUTAGENESIS OF
RP   THR-743.
RX   MEDLINE=99274744; PubMed=10341243;
RA   Ando K., Oishi M., Takeda S., Iijima K.-I., Isohara T., Nairn A.C.,
RA   Kirino Y., Greengard P., Suzuki T.;
RT   "Role of phosphorylation of Alzheimer's amyloid precursor protein
RT   during neuronal differentiation.";
RL   J. Neurosci. 19:4421-4427(1999).
RN   [16]
RP   PHOSPHORYLATION ON THR-743.
RX   PubMed=10936190;
RA   Iijima K.-I., Ando K., Takeda S., Satoh Y., Seki T., Itohara S.,
RA   Greengard P., Kirino Y., Nairn A.C., Suzuki T.;
RT   "Neuron-specific phosphorylation of Alzheimer's beta-amyloid precursor
RT   protein by cyclin-dependent kinase 5.";
RL   J. Neurochem. 75:1085-1091(2000).
RN   [17]
RP   CARBOHYDRATE STRUCTURE OF APPICAN.

RX   PubMed=11479316;
RA   Tsuchida K., Shioi J., Yamada S., Boghosian G., Wu A., Cai H.,
RA   Sugahara K., Robakis N.K.;
RT   "Appican, the proteoglycan form of the amyloid precursor protein,
RT   contains chondroitin sulfate E in the repeating disaccharide region
RT   and 4-O-sulfated galactose in the linkage region.";
RL   J. Biol. Chem. 276:37155-37160(2001).
CC   -!- FUNCTION: Functions as a cell surface receptor and performs
CC   physiological functions on the surface of neurons relevant to
CC   neurite growth, neuronal adhesion and axonogenesis. Involved in
CC   cell mobility and transcription regulation through protein-protein
CC   interactions (By similarity). Can promote transcription activation
CC   through binding to APBB1/Tip60 and inhibit Notch signaling through
CC   interaction with Numb (By similarity). Couples to apoptosis-
CC   inducing pathways such as those mediated by G(O) and JIP. Inhibits
CC   G(O) alpha ATPase activity. Acts as a kinesin I membrane receptor,
CC   mediating the axonal transport of beta-secretase and presenilin 1
CC   (By similarity). May be involved in copper homeostasis/oxidative
CC   stress through copper ion reduction. Can regulate neurite
CC   outgrowth through binding to components of the extracellular
CC   matrix such as heparin and collagen I and IV (By similarity). The
CC   splice isoforms that contain the BPTI domain possess protease
CC   inhibitor activity (By similarity).
CC   -!- FUNCTION: Beta-amyloid peptides are lipophilic metal chelators
CC   with metal-reducing activity. Bind transient metals such as
CC   copper, zinc and iron. Rat and mouse beta-amyloid peptides bind
CC   only weakly transient metals and have little reducing activity due
CC   to substitutions of transient metal chelating residues. Beta-APP42
CC   may activate mononuclear phagocytes in the brain and elicit
CC   inflammatory responses. Promotes both tau aggregation and TPK II-
CC   mediated phosphorylation (By similarity).
CC   -!- FUNCTION: Appicans elicit adhesion of neural cells to the
CC   extracellular matrix and may regulate neurite outgrowth in the
CC   brain.
CC   -!- FUNCTION: The gamma-CTF peptides as well as the caspase-cleaved
CC   peptides, including C31, are potent enhancers of neuronal
CC   apoptosis (By similarity).
CC   -!- SUBUNIT: Binds, via its C-terminal, to the PID domain of several
CC   cytoplasmic proteins, including APBB family members, the APBA
CC   family, MAPK8IP1, SHC1 and Numb and Dab1 (By similarity). Binding
CC   to Dab1 inhibits its serine phosphorylation (By similarity). Also
CC   interacts with GPCR-like protein BPP, FPRL1, APPBP1, IB1, KNS2
CC   (via its TPR domains), APPBP2 (via BaSS) (By similarity) and DDB1.
CC   In vitro, it binds MAPT via the MT-binding domains (By
CC   similarity). Associates with microtubules in the presence of ATP
CC   and in a kinesin-dependent manner (By similarity). Interacts,
CC   through a C-terminal domain, with GNAO1. Amyloid beta-42 binds
CC   CHRNA7 in hippocampal neurons (By similarity). Beta-amyloid
CC   associates with HADH2 (By similarity).
CC   -!- SUBCELLULAR LOCATION: Type I membrane protein. Cell surface
CC   protein that rapidly becomes internalized via clatherin-coated
CC   pits. During maturation, the immature APP (N-glycosylated in the

Query Match   89.8%; Score 44; DB 1; Length 770;
Best Local Similarity   100.0%; Pred. No. 0.26;
Matches   9; Conservative   0; Mismatches   0; Indels   0; Gaps   0;

```
Qy          1 SEVKMDAEF 9
              | | | | | | | | |
Db        667 SEVKMDAEF 675


RESULT 13
T2S1_STRFI
ID   T2S1_STRFI      STANDARD;      PRT;    269 AA.
AC   O52512;
DT   16-OCT-2001 (Rel. 40, Created)
DT   16-OCT-2001 (Rel. 40, Last sequence update)
DT   15-SEP-2003 (Rel. 42, Last annotation update)
DE   Type II restriction enzyme SfiI (EC 3.1.21.4) (Endonuclease SfiI)
DE   (R.SfiI).
GN   SFIIR.
OS   Streptomyces fimbriatus.
OC   Bacteria; Actinobacteria; Actinobacteridae; Actinomycetales;
OC   Streptomycineae; Streptomycetaceae; Streptomyces.
OX   NCBI_TaxID=68197;
RN   [1]
RP   SEQUENCE FROM N.A.
RA   van Cott E.M., Moran L.S., Slatko B.E., Wilson G.G.;
RT   "Characterization of the SfiI restriction and modification genes.";
RL   Submitted (DEC-1997) to the EMBL/GenBank/DDBJ databases.
CC   -!- FUNCTION: Recognizes the double-stranded sequence GGCCNNNNNGGCC
CC       and cleaves before N-9.
CC   -!- CATALYTIC ACTIVITY: Endonucleolytic cleavage of DNA to give
CC       specific double-stranded fragments with terminal 5'-phosphates.
CC   --------------------------------------------------------------------
CC   This SWISS-PROT entry is copyright. It is produced through a collaboration
CC   between  the Swiss Institute of Bioinformatics  and the  EMBL outstation -
CC   the European Bioinformatics Institute.  There are no  restrictions on  its
CC   use  by  non-profit  institutions as long  as its content  is  in  no  way
CC   modified and this statement is not removed.  Usage  by  and for commercial
CC   entities requires a license agreement (See http://www.isb-sib.ch/announce/
CC   or send an email to license@isb-sib.ch).
CC   --------------------------------------------------------------------
DR   EMBL; AF039750; AAB95365.1; -.
DR   REBASE; 1655; SfiI.
KW   Restriction system; Hydrolase; Nuclease; Endonuclease.
SQ   SEQUENCE   269 AA;   31044 MW;   3C48499BAA5205EA CRC64;

  Query Match              75.5%;  Score 37;  DB 1;  Length 269;
  Best Local Similarity    70.0%;  Pred. No. 2.6;
  Matches     7;  Conservative    2;  Mismatches    1;  Indels    0;  Gaps    0;

Qy          1 SEVKMDAEFR 10
              |::  | | | | | |
Db        115 SQLPMDAEFR 124


RESULT 14
PGCV_CHICK
ID   PGCV_CHICK      STANDARD;      PRT;   3562 AA.
AC   Q90953; Q90945;
DT   01-NOV-1997 (Rel. 35, Created)
DT   01-NOV-1997 (Rel. 35, Last sequence update)
```

DE   Versican core protein precursor (Large fibroblast proteoglycan)
DE   (Chondroitin sulfate proteoglycan core protein 2) (PG-M).
GN   CPSG2.
OS   Gallus gallus (Chicken).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC   Archosauria; Aves; Neognathae; Galliformes; Phasianidae; Phasianinae;
OC   Gallus.
OX   NCBI_TaxID=9031;
RN   [1]
RP   SEQUENCE FROM N.A. (ISOFORMS V0 AND V1).
RC   STRAIN=White leghorn; TISSUE=Limb bud;
RX   MEDLINE=93300846; PubMed=8314802;
RA   Shinomura T., Nishida Y., Ito K., Kimata K.;
RT   "cDNA cloning of PG-M, a large chondroitin sulfate proteoglycan
RT   expressed during chondrogenesis in chick limb buds. Alternative
RT   spliced multiforms of PG-M and their relationships to versican.";
RL   J. Biol. Chem. 268:14461-14469(1993).
CC   -!- FUNCTION: May play a role in intercellular signaling and in
CC   connecting cells with the extracellular matrix. May take part in
CC   the regulation of cell motility, growth and differentiation. Binds
CC   hyaluronic acid.
CC   -!- SUBCELLULAR LOCATION: Secreted; extracellular matrix.
CC   -!- ALTERNATIVE PRODUCTS:
CC   Event=Alternative splicing; Named isoforms=2;
CC   Comment=Additional isoforms seem to exist;
CC   Name=V0;
CC   IsoId=Q90953-1; Sequence=Displayed;
CC   Name=V1;
CC   IsoId=Q90953-2; Sequence=VSP_003093;
CC   -!- TISSUE SPECIFICITY: Prechondrogenic condensation area of
CC   developing limb buds.
CC   -!- DEVELOPMENTAL STAGE: Disappears after the cartilage development
CC   (By similarity).
CC   -!- SIMILARITY: Contains 1 immunoglobulin-like V-type domain.
CC   -!- SIMILARITY: Contains 2 link domains.
CC   -!- SIMILARITY: Contains 2 EGF-like domains.
CC   -!- SIMILARITY: Contains 1 C-type lectin family domain.
CC   -!- SIMILARITY: Contains 1 Sushi (SCR) domain.
CC   --
CC   --
DR   EMBL; X60226; CAA42787.1; -.
DR   EMBL; D13542; BAA02742.1; -.
DR   PIR; A47171; A47171.
DR   HSSP; P00740; 1EDM.
DR   InterPro; IPR000152; Asx_hydroxyl.
DR   InterPro; IPR000742; EGF_2.
DR   InterPro; IPR001881; EGF_Ca.
DR   InterPro; IPR006209; EGF_like.
DR   InterPro; IPR007110; Ig-like.

```
DR    InterPro; IPR003599; Ig.
DR    InterPro; IPR003006; Ig_MHC.
DR    InterPro; IPR001304; Lectin_C.
DR    InterPro; IPR000538; Link.
DR    InterPro; IPR000436; Sushi_SCR_CCP.
DR    Pfam; PF00008; EGF; 2.
DR    Pfam; PF00047; ig; 1.
DR    Pfam; PF00059; lectin_c; 1.
DR    Pfam; PF00084; sushi; 1.
DR    Pfam; PF00193; Xlink; 2.
DR    PRINTS; PR01265; LINKMODULE.
DR    ProDom; PD000918; Link; 2.
DR    SMART; SM00032; CCP; 1.
DR    SMART; SM00034; CLECT; 1.
DR    SMART; SM00179; EGF_CA; 1.
DR    SMART; SM00409; IG; 1.
DR    SMART; SM00445; LINK; 2.
DR    PROSITE; PS00010; ASX_HYDROXYL; 1.
DR    PROSITE; PS00615; C_TYPE_LECTIN_1; 1.
DR    PROSITE; PS50041; C_TYPE_LECTIN_2; 1.
DR    PROSITE; PS00022; EGF_1; 2.
DR    PROSITE; PS01186; EGF_2; 1.
DR    PROSITE; PS01187; EGF_CA; 1.
DR    PROSITE; PS50835; IG_LIKE; 1.
DR    PROSITE; PS01241; LINK; 2.
KW    Glycoprotein; Proteoglycan; Lectin; Extracellular matrix; Sushi;
KW    Signal; Repeat; EGF-like domain; Calcium; Immunoglobulin domain;
KW    Hyaluronic acid; Alternative splicing.
FT    SIGNAL        1     26         POTENTIAL.
FT    CHAIN        27   3562         VERSICAN CORE PROTEIN.
FT    DOMAIN       27    143         IG-LIKE V-TYPE.
FT    DOMAIN      166    243         LINK 1.
FT    DOMAIN      264    345         LINK 2.
FT    DOMAIN     3254   3290         EGF-LIKE 1.
FT    DOMAIN     3292   3328         EGF-LIKE 2, CALCIUM-BINDING (POTENTIAL).
FT    DOMAIN     3341   3455         C-TYPE LECTIN.
FT    DOMAIN     3460   3518         SUSHI.
FT    DISULFID     44    129         BY SIMILARITY.
FT    DISULFID    171    242         BY SIMILARITY.
FT    DISULFID    195    216         BY SIMILARITY.
FT    DISULFID    269    344         BY SIMILARITY.
FT    DISULFID    293    314         BY SIMILARITY.
FT    DISULFID   3258   3269         BY SIMILARITY.
FT    DISULFID   3263   3278         BY SIMILARITY.
FT    DISULFID   3280   3289         BY SIMILARITY.
FT    DISULFID   3296   3307         BY SIMILARITY.
FT    DISULFID   3301   3316         BY SIMILARITY.
FT    DISULFID   3318   3327         BY SIMILARITY.
FT    DISULFID   3334   3345         BY SIMILARITY.
FT    DISULFID   3362   3454         BY SIMILARITY.
FT    DISULFID   3430   3446         BY SIMILARITY.
FT    DISULFID   3461   3504         BY SIMILARITY.
FT    DISULFID   3490   3517         BY SIMILARITY.
FT    CARBOHYD    163    163         N-LINKED (GLCNAC. . .) (POTENTIAL).
FT    CARBOHYD    235    235         N-LINKED (GLCNAC. . .) (POTENTIAL).
FT    CARBOHYD    329    329         N-LINKED (GLCNAC. . .) (POTENTIAL).
FT    CARBOHYD    529    529         N-LINKED (GLCNAC. . .) (POTENTIAL).
```

```
FT   CARBOHYD    709    709      N-LINKED (GLCNAC. . .) (POTENTIAL).
FT   CARBOHYD    948    948      N-LINKED (GLCNAC. . .) (POTENTIAL).
FT   CARBOHYD   1409   1409      N-LINKED (GLCNAC. . .) (POTENTIAL).
FT   CARBOHYD   1479   1479      N-LINKED (GLCNAC. . .) (POTENTIAL).
FT   CARBOHYD   1523   1523      N-LINKED (GLCNAC. . .) (POTENTIAL).
FT   CARBOHYD   1530   1530      N-LINKED (GLCNAC. . .) (POTENTIAL).
FT   CARBOHYD   1625   1625      N-LINKED (GLCNAC. . .) (POTENTIAL).
FT   CARBOHYD   1751   1751      N-LINKED (GLCNAC. . .) (POTENTIAL).
FT   CARBOHYD   1988   1988      N-LINKED (GLCNAC. . .) (POTENTIAL).
FT   CARBOHYD   2088   2088      N-LINKED (GLCNAC. . .) (POTENTIAL).
FT   CARBOHYD   2089   2089      N-LINKED (GLCNAC. . .) (POTENTIAL).
FT   CARBOHYD   2507   2507      N-LINKED (GLCNAC. . .) (POTENTIAL).
FT   CARBOHYD   2642   2642      N-LINKED (GLCNAC. . .) (POTENTIAL).
FT   CARBOHYD   2679   2679      N-LINKED (GLCNAC. . .) (POTENTIAL).
FT   CARBOHYD   2748   2748      N-LINKED (GLCNAC. . .) (POTENTIAL).
FT   CARBOHYD   2762   2762      N-LINKED (GLCNAC. . .) (POTENTIAL).
FT   CARBOHYD   3069   3069      N-LINKED (GLCNAC. . .) (POTENTIAL).
FT   CARBOHYD   3194   3194      N-LINKED (GLCNAC. . .) (POTENTIAL).
FT   CARBOHYD   3232   3232      N-LINKED (GLCNAC. . .) (POTENTIAL).
FT   CARBOHYD   3545   3545      N-LINKED (GLCNAC. . .) (POTENTIAL).
FT   VARSPLIC    485   1411      Missing (in isoform V1).
FT                              /FTId=VSP_003093.
SQ   SEQUENCE   3562 AA;   388078 MW;   9BC566E88C1602D2 CRC64;
```

Query Match   69.4%;   Score 34;   DB 1;   Length 3562;
Best Local Similarity   66.7%;   Pred. No. 1.4e+02;
Matches   6;   Conservative   2;   Mismatches   1;   Indels   0;   Gaps   0;

```
Qy         1 SEVKMDAEF 9
             | :|:||||
Db      1709 STIKLDAEF 1717
```


RESULT 15
APB_HUMAN
```
ID   APB_HUMAN      STANDARD;      PRT;   4563 AA.
AC   P04114; O00502; Q13787;
DT   01-NOV-1986 (Rel. 03, Created)
DT   01-NOV-1986 (Rel. 03, Last sequence update)
DT   28-FEB-2003 (Rel. 41, Last annotation update)
DE   Apolipoprotein B-100 precursor (Apo B-100) [Contains: Apolipoprotein
DE   B-48 (Apo B-48)].
GN   APOB.
OS   Homo sapiens (Human).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC   Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
OX   NCBI_TaxID=9606;
RN   [1]
RP   SEQUENCE FROM N.A.
RX   MEDLINE=87016385; PubMed=3763409;
RA   Knott T.C., Wallis S.C., Powell L.M., Pease R.J., Lusis A.J.,
RA   Blackhart B., McCarthy B.J., Mahley R.W., Levy-Wilson B., Scott J.;
RT   "Complete cDNA and derived protein sequence of human apolipoprotein
RT   B-100.";
RL   Nucleic Acids Res. 14:7501-7503(1986).
RN   [2]
RP   SEQUENCE FROM N.A.
```

RX   MEDLINE=88003974; PubMed=3652907;
RA   Ludwig E.H., Blackhart B.D., Pierotti V.R., Caiati L., Fortier C.,
RA   Knott T., Scott J., Mahley R.W., Levy-Wilson B., McCarthy B.J.;
RT   "DNA sequence of the human apolipoprotein B gene.";
RL   DNA 6:363-372(1987).
RN   [3]
RP   SEQUENCE FROM N.A.
RX   MEDLINE=87008488; PubMed=3759943;
RA   Chen S.-H., Yang C.-Y., Chen P.-F., Setzer D., Tanimura M., Li W.-H.,
RA   Gotto A.M. Jr., Chan L.;
RT   "The complete cDNA and amino acid sequence of human apolipoprotein
RT   B-100.";
RL   J. Biol. Chem. 261:12918-12921(1986).
RN   [4]
RP   SEQUENCE FROM N.A.
RX   MEDLINE=87041416; PubMed=3464946;
RA   Law S.W., Grant S.M., Higuchi K., Hospattankar A.V., Lackner K.J.,
RA   Lee N., Brewer H.B. Jr.;
RT   "Human liver apolipoprotein B-100 cDNA: complete nucleic acid and
RT   derived amino acid sequence.";
RL   Proc. Natl. Acad. Sci. U.S.A. 83:8142-8146(1986).
RN   [5]
RP   SEQUENCE FROM N.A.
RX   MEDLINE=87161758; PubMed=3030729;
RA   Cladaras C., Hadzopoulou-Cladaras M., Nolte R.T., Atkinson D.,
RA   Zannis V.I.;
RT   "The complete sequence and structural analysis of human
RT   apolipoprotein B-100: relationship between apoB-100 and apoB-48
RT   forms.";
RL   EMBO J. 5:3495-3507(1986).
RN   [6]
RP   SEQUENCE OF 709-906 FROM N.A.
RX   MEDLINE=85270450; PubMed=3860836;
RA   Deeb S.S., Motulsky A.G., Albers J.J.;
RT   "A partial cDNA clone for human apolipoprotein B.";
RL   Proc. Natl. Acad. Sci. U.S.A. 82:4983-4986(1985).
RN   [7]
RP   SEQUENCE OF 3056-3159 FROM N.A.
RX   MEDLINE=86041888; PubMed=3903660;
RA   Mehrabian M., Schumaker V.N., Fareed G.C., West R., Johnson D.F.,
RA   Kirchgessner T.G., Lin H.-C., Wang X., Ma Y., Mendiaz E., Lusis A.J.;
RT   "Human apolipoprotein B: identification of cDNA clones and
RT   characterization of mRNA.";
RL   Nucleic Acids Res. 13:6937-6953(1985).
RN   [8]
RP   SEQUENCE OF 1937-2018 AND 3811-4334 FROM N.A.
RX   MEDLINE=86093680; PubMed=3841204;
RA   Carlsson P., Olofsson S.O., Bondjers G., Darnfors C., Wiklund O.,
RA   Bjursell G.;
RT   "Molecular cloning of human apolipoprotein B cDNA.";
RL   Nucleic Acids Res. 13:8813-8826(1985).
RN   [9]
RP   SEQUENCE OF 3109-4563 FROM N.A.
RX   MEDLINE=85300528; PubMed=2994225;
RA   Knott T.J., Rall S.C. Jr., Innerarity T.L., Jacobson S.F.,
RA   Urdea M.S., Levy-Wilson B., Powell L.M., Pease R.J., Eddy R.,
RA   Nakai H., Byers M., Priestley L.M., Robertson E., Rall L.B.,

RA   Betsholtz C., Shows T.B., Mahley R.W., Scott J.;
RT   "Human apolipoprotein B: structure of carboxyl-terminal domains,
RT   sites of gene expression, and chromosomal localization.";
RL   Science 230:37-43(1985).
RN   [10]
RP   SEQUENCE OF 1-291 FROM N.A.
RX   MEDLINE=86149325; PubMed=3513177;
RA   Protter A.A., Hardman D.A., Schilling J.W., Miller J., Appleby V.,
RA   Chen G.C., Kirsher S.W., McEnroe G., Kane J.P.;
RT   "Isolation of a cDNA clone encoding the amino-terminal region of
RT   human apolipoprotein B.";
RL   Proc. Natl. Acad. Sci. U.S.A. 83:1467-1471(1986).
RN   [11]
RP   SEQUENCE OF 1-1670 FROM N.A.
RX   MEDLINE=86287319; PubMed=3461454;
RA   Protter A.A., Hardman D.A., Sato K.Y., Schilling J.W.,
RA   Yamanaka M., Hort Y.J., Hjerrild K.A., Chen G.C., Kane J.P.;
RT   "Analysis of cDNA clones encoding the entire B-26 region of human
RT   apolipoprotein B.";
RL   Proc. Natl. Acad. Sci. U.S.A. 83:5678-5682(1986).
RN   [12]
RP   PARTIAL SEQUENCE, AND IDENTIFICATION OF APO-B48.
RX   MEDLINE=88018019; PubMed=3659919;
RA   Chen S.-H., Habib G., Yang C.-H., Gu Z.-W., Lee B.R., Weng S.-H.,
RA   Silberman S.R., Cai S.-J., Deslypere J.P., Rosseneu M.,
RA   Gotto A.M. Jr., Li W.-H., Chan L.;
RT   "Apolipoprotein B-48 is the product of a messenger RNA with an organ-
RT   specific in-frame stop codon.";
RL   Science 238:363-366(1987).
RN   [13]
RP   DOMAINS.
RX   MEDLINE=87039351; PubMed=3773997;
RA   Knott T.C., Pease R.J., Powell L.M., Wallis S.C., Rall S.C. Jr.,
RA   Innerarity T.L., Blackhart B., Taylor W.R., Marcel Y., Milne R.,
RA   Johnson D., Fuller M., Lusis A.J., McCarthy B.J., Mahley R.W.,
RA   Levy-Wilson B., Scott J.;
RT   "Complete protein sequence and identification of structural domains
RT   of human apolipoprotein B.";
RL   Nature 323:734-738(1986).
RN   [14]
RP   DOMAINS.
RA   Yang C.-Y., Chen S.-H., Gianturco S.H., Bradley W.A., Sparrow J.T.,
RA   Tanimura M., Li W.-H., Sparrow D.A., Deloof H., Rosseneu M.,
RA   Lee F.-S., Gu Z.-W., Gotto A.M. Jr., Chan L.;
RT   "Sequence, structure, receptor-binding domains and internal repeats
RT   of human apolipoprotein B-100.";
RL   Nature 323:738-742(1986).
RN   [15]
RP   CALCIUM-BINDING DATA.
RX   MEDLINE=86242245; PubMed=3087360;
RA   Dashti N., Lee D.M., Mok T.;
RT   "Apolipoprotein B is a calcium binding protein.";
RL   Biochem. Biophys. Res. Commun. 137:493-499(1986).
RN   [16]
RP   PALMITOYLATION OF CYS-1112.
RX   MEDLINE=20143590; PubMed=10679026;
RA   Zhao Y., McCabe J.B., Vance J., Berthiaume L.G.;

RT   "Palmitoylation of apolipoprotein B is required for proper
RT   intracellular sorting and transport of cholesteroyl esters and
RT   triglycerides.";
RL   Mol. Biol. Cell 11:721-734(2000).
RN   [17]
RP   VARIANT SER-4338.
RX   MEDLINE=91071750; PubMed=1979313;
RA   Navajas M., Laurent A.-M., Moreel J.-F., Ragab A., Cambou J.-P.,
RA   Cunny G., Cambien F., Roizes G.;
RT   "Detection by denaturing gradient gel electrophoresis of a new
RT   polymorphism in the apolipoprotein B gene.";
RL   Hum. Genet. 86:91-93(1990).
RN   [18]
RP   VARIANT FDB GLN-3527.
RX   MEDLINE=89098975; PubMed=2563166;
RA   Soria L.F., Ludwig E.H., Clarke H.R.G., Vega G.L., Grundy S.M.,
RA   McCarthy B.J.;
RT   "Association between a specific apolipoprotein B mutation and
RT   familial defective apolipoprotein B-100.";
RL   Proc. Natl. Acad. Sci. U.S.A. 86:587-591(1989).
RN   [19]
RP   VARIANT LEU-2739.
RX   MEDLINE=91016974; PubMed=2216805;
RA   Huang L.-S., Gavish D., Breslow J.L.;
RT   "Sequence polymorphism in the human apoB gene at position 8344.";
RL   Nucleic Acids Res. 18:5922-5922(1990).
RN   [20]
RP   VARIANT FDB CYS-3558.
RX   MEDLINE=95190020; PubMed=7883971;
RA   Pullinger C.R., Hennessy L.K., Chatterton J.E., Liu W., Love J.A.,
RA   Mendel C.M., Frost P.H., Malloy M.J., Schumaker V.N., Kane J.P.;
RT   "Familial ligand-defective apolipoprotein B. Identification of a new
RT   mutation that decreases LDL receptor binding affinity.";
RL   J. Clin. Invest. 95:1225-1234(1995).
RN   [21]
RP   VARIANTS LEU-1437; SER-1914; LYS-2566; THR-3121; ALA-3945; MET-4128
RP   AND THR-4481.
RX   MEDLINE=97044521; PubMed=8889592;
RA   Poirier O., Ricard S., Behague I., Souriau C., Evans A.E.,
RA   Arveiler D., Marques-Vidal P., Luc G., Roizes G., Cambien F.;
RT   "Detection of new variants in the apolipoprotein B (Apo B) gene by
RT   PCR-SSCP.";
RL   Hum. Mutat. 8:282-285(1996).
RN   [22]
RP   VARIANTS FDB GLN-3527 AND CYS-3558.
RX   MEDLINE=97403938; PubMed=9259199;
RA   Rabes J.P., Varret M., Saint-Jore B., Erlich D., Jondeau G.,
RA   Krempf M., Giraudet P., Junien C., Boileau C.;
RT   "Familial ligand-defective apolipoprotein B-100: simultaneous
RT   detection of the ARG3500-->GLN and ARG3531-->CYS mutations in a
RT   French population.";
RL   Hum. Mutat. 10:160-163(1997).
RN   [23]
RP   VARIANTS SER-1914; ARG-1923; LEU-2739; ASP-3319; THR-3427; GLN-3432
RP   AND ILE-3921.
RX   MEDLINE=98141125; PubMed=9490296;
RA   Leren T.P., Bakken K.S., Hoel V., Hjermann I., Berg K.;

RT   "Screening for mutations of the apolipoprotein B gene causing
RT   hypocholesterolemia.";
RL   Hum. Genet. 102:44-49(1998).
CC   -!- FUNCTION: APOLIPOPROTEIN B IS A MAJOR PROTEIN CONSTITUENT OF
CC   CHYLOMICRONS, VLDL AND LDL. IT FUNCTIONS AS A RECOGNITION SIGNAL
CC   FOR THE CELLULAR BINDING AND INTERNALIZATION OF LDL PARTICLES BY
CC   THE APOB/E RECEPTOR.

  Query Match   69.4%; Score 34; DB 1; Length 4563;
  Best Local Similarity 66.7%; Pred. No. 1.8e+02;
  Matches   6; Conservative   2; Mismatches   1; Indels   0; Gaps   0;

Qy   2 EVKMDAEFR 10
              |||:| :||
Db   1483 EVKIDGQFR 1491

Search completed: January 21, 2004, 09:23:05
Job time : 2.49713 secs